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ORIGINAL ARTICLES

**DIFFERENTIATION OF THE DISEASES INCLUDED UNDER
CHRONIC ARTHRITIS.¹**

BY LEWELLYS F. BARKER, M.D.,

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CONCEPTIONS in internal medicine have in recent years been evolving with unprecedented rapidity. The organization of medical research, the growth of the sciences fundamental to medicine, and the application of physical, chemical, and biological methods to the solution of the problems of physiology and pathology are so widening our knowledge of disease-processes that we are constantly being driven to readjustments, especially in our classifications of disease. Conditions formerly thought to be simple turn out on more exact study to be very complex, and, in turn, a new discovery may prove that conditions hitherto apparently disparate, are, in reality, united by a common bond. Thus, in some instances, our forerunners stand convicted of excessive simplicity of view; in others, of interpretations which were unnecessarily complicated.

The greater the definiteness with which we perceive and deal with our problems, the more steady and satisfactory is the progress toward their solution. Our newer conceptions of the infectious diseases illustrate the point well. Recently, attention has been turned again to the diseases of the individual organs with the hope of diminishing their vagueness. That this has not been without success, the newer studies of the cardiopathies and the nephro-

¹ Read, as one of two Reports on the subject, before the Section on Medicine of the International Medical Congress, London, August, 9, 1913; the other Report made by Professor Fr. v. Müller, of Munich, is to be published in Volkmann's klinische Beiträge.

pathies attest. And when we turn to the diseases of the joints (or arthropathies), including the diseases comprised under "chronic arthritis," the subject with which this report² is to deal, it is gratifying to find that, out of apparent chaos, definite forms are emerging; the discouragement felt at the utter confusion which formerly prevailed is giving way to hopefulness as well-characterized clinical syndromes appear, as anatomical changes revealed by the x -rays, at operation or at autopsy, assume distinct shape, and, especially, as etiological studies yield us patterns upon which positive conceptions of pathogenesis can be moulded. But despite the real progress which has been made, it must be confessed that the arthropathies are still veiled in deplorable obscurity. No one who reviews the bibliography of our own time can ignore it. And, as we shall see, the dimness, while due chiefly to our inability as yet, except in certain instances, to look at the processes from an etiological viewpoint, is to some extent dependent upon an intervening dust-cloud of terminology. In no part of medicine, perhaps, have *names* been used less satisfactorily than in designating the arthropathies; we find, on the one hand, one malady masquerading under many different names, or, on the other hand, one name used ambiguously, meaning sometimes one disease, sometimes another, or sometimes a group of separable diseases. Even today there are scarcely two authors in one country who use precisely the same terminology for the arthropathies; add to this the varying use of terms by writers of different nationalities and the lack of uniformity of expression becomes very perplexing. Notwithstanding, however, all the confusion which exists regarding names, a study of their history will reveal the fact that the introduction of each corresponded to some special conception, and that, for the purpose for which it was chosen, it usually served a useful function. The difficulties which have arisen have been largely due to the attempts made to force classifications and names made for different purposes into coincidence with one another. Ignoring the original purpose of a name, writers not infrequently use it for a wholly different purpose, with subsequent disorder and excitation of controversy. A comparison of the cases of joint diseases with which one is familiar in America with the cases described by writers in Great Britain, Germany, Austria, and France makes it clear that the material in different countries is not dissimilar. In an International Medical Congress like this it would seem fitting thoroughly to discuss the types now everywhere known, and to try to come to a general agreement as to the terms which may best be employed in describing them.

² This report is based upon (1) personal experience with the arthropathies in the medical clinic of the Johns Hopkins Hospital (1905-12); (2) a study of the bibliography; and (3) many consultations with my colleagues in the medical, surgical, and radiographic departments of the hospital.

To understand the origin of the many names now used for the various diseases included under "chronic arthritis," some acquaintance with the development of our knowledge of diseases of the joints, both acute and chronic, is indispensable. The diseases are not new. Bones, thousands of years old, have been found in Egypt which show unmistakable signs of deforming pathological processes in the joints (Page May). The ancient authors (*cf.* Scribonius Largus, A.D. 41)³ used the term *ἀρθριτις* for acute diseases of the joints (like acute rheumatic fever), and the term *ποδάγρα* for gout; they seem also to have been familiar with chronic joint diseases other than gout. The term *rheumatism* (Lat. *rheumatismus* = Greek *ῥευματισμός*) meant liability to "rheum" and dates back to times when physicians believed that harmful phlegm flowed down from the brain and injured other organs of the body, a part of the humoral pathology which had adherents until the latter half of the seventeenth century; "rheumatism" seems to have been used, at first, as a name for some of the complications of gout. At the end of the sixteenth century, G. D. Baillou, a contemporary of Rabelais, reversed the ancient usage of the word *arthritis*, applying it to the gouty affections, and the word *rheumatism* to the acute diseases of joints. As early as 1683, Sydenham distinguished "chronic rheumatism" (rheumatism not accompanied by fever) from "gout," asserting that they are essentially different diseases.⁴

In the year 1800, in a Paris Thesis, Landré-Beauvais separated from true gout a condition to which he gave the name "primary asthenic gout" (*goutte asthénique primitive*), stating that it affects chiefly females, has a chronic course, and leads to enlargement and deformity of the joints, without tophi. The same disease was recognized by William Heberden, the elder (1710-1801), and carefully described by him in his famous *Commentaries*; at the same time he described as *digitorum nodi* the nodes (which bear his name) on the distal joints of the fingers. Just a little later (1805) appeared the memoir by John Haygarth, entitled *A Clinical History of Diseases*, part first being (1) A Clinical History of the Acute Rheumatism, (2) A Clinical History of the Nodosity of the Joints. In the first half of the nineteenth century, the French writers referred to the chronic non-suppurative joint diseases as "gouty rheumatism" (*rhumatisme goutteux*), and as "dry arthritis" (*arthrite sèche*); at about the middle of the century the terms "rheumatic gout" (Fuller, 1852) and "chronic rheumatic arthritis" (Adams, 1857) attained to considerable vogue in Great Britain. Soon after this, three names began to be employed which were

³ Cited by Pribram in his admirable article in Nothnagel's System.

⁴ That an attempt to make classifications more elaborate than the facts justify is not a failing peculiar to our times is shown by the fifteen varieties of chronic rheumatism described by de Sauvage and the thirty-four varieties differentiated by Cullen.

destined to play an important role in the terminology: (1) "primary progressive chronic articular rheumatism" (Charcot, 1853; Vidal, 1855), (2) "rheumatoid arthritis" (Garrod, 1859), and (3) "arthritis deformans" (Virchow, 1869). The first of the three names indicated the growing tendency to distinguish among the chronic non-gouty diseases of the joints a form that is primary (that is, chronic from the beginning), and a form that is secondary (that is, a chronic following an acute process); and the last of these three names referred to the marked changes in the bones and cartilages found at autopsy in certain cases of chronic joint disease. Virchow used "arthritis deformans" in an anatomical sense; it has since been used also in a clinical sense, but unfortunately in various ways. The adjective "deformans" is ambiguous, some authors having deformities of bones in mind (osteoarthritis deformans), others thinking instead of the pathological "deviations" due to contractures or other causes. In Germany the surgeons (R. von Volkmann, Schuchardt, Hoffa), and some internists (Schüller, Příbram, W. His), have distinguished sharply, as "arthritis deformans" or "osteoarthritis deformans," a disease monoarticular or oligoarticular in type, coming on slowly, usually in advanced life, never leading to true ankylosis, and presenting anatomically (and in x-ray pictures) extensive exostoses, especially at the edges of the articular cartilages; they do not include under "arthritis deformans" the other non-gouty joint-diseases, but group many of the latter together as "chronic articular rheumatism" (*chronischer Gelenkrheumatismus*), in turn subdivided into several groups (*vide infra*) and including the "primary chronic progressive polyarthritis" (*polyarthritis chronica progressiva primitiva* [His, A. Hoffa]). Some German writers, especially internists like Curschmann and Bäumler, have opposed the sharp separation of "arthritis deformans" from "primary progressive polyarthritis;" they include both under terms like "polyarthritis chronica deformans."

In America, Goldthwaite (1904), whose conceptions of the arthropathies have strongly influenced American workers, discarded the term "arthritis deformans," and, in addition to "chronic infectious arthritis," used the terms "hypertrophic osteoarthritis" (= "osteoarthritis deformans") and "atrophic arthritis" (= "primary progressive chronic polyarthritis"). These names have been extensively used by Painter, Osgood, Bacr, and Fayerweather. Nathan (1906) uses a similar terminology, but extends it considerably in an effort to value clinically the results of studies in pathological anatomy. T. McCrae, in his exhaustive analysis in Osler's *Modern Medicine* (1909), uses the term "arthritis deformans" to include only cases of chronic arthritic change in which no definite etiological factor can be found, but he subdivides this great group into three main sub-groups, of which the first or "peri-

articular form" and the second or "atrophic form" appear to correspond (in part at least) to the "primary chronic progressive polyarthritis" above mentioned, while his third or "hypertrophic form" corresponds to the "osteoarthritis deformans" described above.

In Great Britain, the terminology used can be found in the excellent treatises of Sir A. B. Garrod (1876), A. E. Garrod (1890) Bannatyne (1896), Spender (1897), and Hale White (1902). Recently, A. E. Garrod (1910), in Albutt and Rolleston's *System*, has sharply distinguished (1) "osteoarthritis" (= "osteoarthritis deformans") from (2) "rheumatoid arthritis" (= "primary chronic progressive polyarthritis") and from (3) the "articular lesions of infectious diseases." The whole subject of the chronic arthropathies is being further illuminated in England through the investigations of the Committee for the Study of Special Diseases at Cambridge; the reports of Strangeways and Nicholson and their associates in the *Bulletins* of the Committee are a mine of information for all who are interested in chronic arthritis.

In France, Lancereaux (1888) used "chronic rheumatism" or "herpetism" as a general term, subdividing it into (a) "generalized chronic articular rheumatism" (= primary chronic progressive polyarthritis + chronic arthropathies secondary to acute processes) and (b) "partial chronic rheumatic arthritis" (= osteoarthritis deformans), including a form with effusion and a dry form; this classification closely resembles Charcot's (1889) subdivision into (a) "chronic progressive articular rheumatism" and (b) "chronic partial rheumatism." Pierre Marie (1896) used the terms (a) *rhumatisme chronique déformant arthrique ou diathésique* (= (in part) osteoarthritis deformans) and (b) *rhumatisme chronique déformant infectieux* (chronic arthritis following infectious processes). In the latter group he appears to include the cases of "primary chronic progressive polyarthritis." In 1896 Chauffard and Ramon also emphasized the conception of "chronic infectious arthritis" (= *rhumatisme chronique infectieux*), and in the same year Barbazon used the name "pernicious arthritis." Tessier and Roque (1897), under "chronic deforming rheumatism" (*rhumatisme chronique déformant*), include both *rhumatisme chronique progressif* (= primary chronic progressive polyarthritis) and *rhumatisme chronique partiel* (= osteoarthritis deformans).

Doubtless a familiarity with Italian and Russian literature, which, unfortunately, I do not possess, would reveal corresponding similarities and discrepancies.⁵ Everywhere clinicians are obviously dealing with identical forms; to recognize them one has only to study the accounts of the cases, taking care not to be confused by the names attached to them.

⁵ The review of the subject by Predtetschensky (1902) indicates that in Russia the same problems have to be met by clinicians.

GRADUAL RESTRICTION OF MEANING OF THE TERMS "GOUT," "ARTHRITIS," "RHEUMATISM," AND "ARTHRITIS DEFORMANS."

The brief historical notes given above indicate in a broad way the gradual alteration which, in the progress from vagueness toward definiteness, some of the conceptions and terms bearing upon joint diseases have undergone. At present, there is a still greater tendency to restriction and precision. In the minds of the laity the ideas which prevail are, it is true, still very hazy, "rheumatism" on the whole meaning to the man in the street something rather mild, "arthritis" something more severe, "gout" something reprehensible; but in the minds of medical men the same terms are attaining to more exact definition as the distinctions among joint diseases are becoming more clearly drawn on the ground of essential differences. As is always the case, however, where distinctions are not yet wholly firm and clear, it is difficult to know just how much those which we try to make are worth. Scientific men have had so many lessons in the unsatisfactoriness of "hard-and-fast distinctions" that they are prone to be shy in adopting them; they have so often had difficulty with the exceptional and puzzling cases which occupy a region intermediate between two opposed classes that they are skeptical when attempts at rigid definition are made. Still, all will grant that, to overcome ambiguity and vagueness, we must make use of classification, involving distinctions and definitions. And, moreover, no small part of our progress in medicine depends upon the disputes which arise between opposing parties as to the value of the distinctions made. One side may see only the value of a distinction and be blind to its defects; the other side may think the difference on which the distinction is made between two classes unimportant, asserting that, on the contrary, the resemblance is essential. We have a good example of this in the discussions which have arisen regarding the term "arthritis deformans;" they are resulting gradually in the use of distinctions which prevent certain important confusions into which we formerly fell.

The history of the arthropathies is as convincing as anything can be that the value of a given classification changes with circumstances as well as with times. Thus, the distinctions made at the period when Thomas Sydenham or Sir Benjamin Brodie worked, though most useful then, are obviously insufficient now. Furthermore, the distinctions which, today, the morbid anatomist needs, and which suffice for his purposes, may be very different from those necessary for, or sufficient for, the clinician in his work, or the etiologist in his studies. The *purpose* of a given name, or a given classification, should always be definitely understood. In medicine we have, at all times, to work in a world of rough distinctions, and medical men, perhaps more than most, have ever to be on

guard against the fallacies into which, through the imperfections of their distinctions, they may be misled. The importance of such considerations for an understanding of the difficulties of terminology which beset the study of the arthropathies, will, I trust, be sufficient excuse for the digression just made.

We may now turn to the tendencies at present noticeable in defining the terms "gout," "arthritis," and "rheumatism." There seems to be, at present, general agreement that the word "gout" shall be applied only to processes dependent upon abnormalities of the metabolism of purins. In the "gouty" arthropathy (*A. urica*) there is an excess of uric acid in the blood and a tendency to tophaceous deposits in the tissues. The accompanying clinical phenomena in "typical" gout are so characteristic as to permit of easy recognition, though in "atypical" cases there may be great difficulty in distinguishing gout from other diseases. At present, the tendency to avoid the use of the words "gout," and "goutiness" in describing diseases in which we have no evidence of abnormal purin metabolism seems to be universal; this accounts for the general abandonment of terms like "primary asthenic gout," "rheumatic gout," and "gouty rheumatism."

There is much more disagreement as to the use of the word "arthritis." Originally used in the sense of "acute joint-disease," it came in the sixteenth century to be limited rather to gout. In modern times it has been used almost in the general sense of "joint-disease" or "arthropathy," though a tendency, without good reason, to separate acute rheumatic fever and, to a certain extent, gout from the designation "arthritis" has been noticeable. If I judge the present tendency aright, it is to apply the term "arthritis" (and to limit it) to true inflammation of the joints in the sense of the pathological anatomists, that is, to all inflammatory arthropathies, acute and chronic, including (1) the arthritis of acute rheumatic fever and of other infections, and (2) all forms of chronic joint inflammation (including the gouty), but excluding the non-inflammatory arthropathies (for example, the purely degenerative).

More confusing still are the uses made of the words "rheumatism" and "rheumatic." Though most often employed in naming joint diseases, they have also been applied to diseases of other parts (muscles, serous membranes, eyes, throat, brain, nerves, etc.), diseases presumably due to the same causes as those producing the joint-diseases so named.

We have seen how "rheumatism" was first used to name diseases resulting from the flow of phlegm from the brain, how "rheumatism" and "gout" were first sharply distinguished by Baillou (1538-1616), how the non-gouty joint-diseases were divided into "acute rheumatism" and "chronic rheumatism" by Sydenham (1624-89), and how "chronic rheumatism" began to be divided into a "primary form" (chronic from the first), and a "secondary form" (following the "acute") by various writers, beginning with Landré-Beauvais (1800) and made clearer later by Heberden,

Haygarth, Charcot, Vidal, Jaccoud, and others. In order to understand current tendencies in defining "chronic rheumatism," the changes of fortune undergone by the term "acute rheumatism" must first be glanced at. For a long time "acute rheumatism" appears to have meant simply any acute arthropathy not traumatic or gouty in its origin. But gradually it has come to mean an acute febrile polyarticular affection, frequently complicated by endocarditis, pericarditis, or chorea, not leading to suppuration of the joint, but responding promptly to treatment with salicylates, and ending in recovery without residual joint change. It is interesting on examining the texts of Sir B. Brodie (1818), A. Bonnet (1845), E. Gurlt (1853), and R. von Volkmann (1882), to find how skillfully, before the advent of modern bacteriological studies, clinicians were able to separate acute articular rheumatism (*rhumatisme articulaire aigu*, *akuter Gelenkrheumatismus*) not only from (1) the pyæmic joint affections, but also from (2) gonorrheal rheumatism (*Rheumatismus urethralis*; *Tripperrheumatismus*; *arthromeningitis gonorrhoeica*)⁶ and (3) the polyarthritides complicating the acute exanthems, typhoid, dysentery, mumps, syphilis, etc. Hence it does not surprise us that when, after bacteriological studies, acute infectious arthritis came to be better understood, the acute non-suppurative, polyarticular joint-diseases resembling acute rheumatic fever, but differing from it in several important particulars (cause, course, occasional suppuration, relative inefficacy of salicylates), began to be grouped together as "pseudorheumatisms" (Bouchard) or as "rheumatoids" (Gerhardt). When the bacteria causing a given pseudorheumatism could be determined, a corresponding special name was applied (for example, Polyarthritis gonococcica, *P. streptococcica*, *P. staphylococcica*, *P. pneumococcica*). With the rise of this doctrine of the "pseudorheumatisms," the question again arose as to the existence after all of a true "acute articular rheumatism" in the narrower sense. Thus it was asked, Does not the whole series of pseudorheumatisms, taken together, account for everything known as "acute rheumatism?" Today no one longer questions the independence of "acute rheumatic fever" (*polyarthritis rheumatica acuta*) though its etiology is still entirely unknown.⁷ Still, it is looked upon as a definite

⁶ This was described carefully by Musgrave as early as 1723.

⁷ A number of bacteria have been described as the cause of acute rheumatic fever (Mantle, Sahli, Poynton and Paine), but the majority of investigators have had negative results from cultures made from the blood and joints. In the medical clinic of the Johns Hopkins Hospital a large number of blood cultures have been made in acute rheumatic fever (true) by competent bacteriologists (R. I. Cole, B. Cohoe, F. J. Sladen, P. W. Clough, C. G. Guthrie, C. R. Austrian, R. Major, and T. P. Sprunt) with uniformly negative results. Very recently, E. C. Rosenow, of Chicago, has been able by use of an ascites-dextrose-agar medium to obtain bacterial growths (micrococci; diplococci; streptococci) from a majority of cases of "acute rheumatic fever;" the bacteria will not, at first, grow under either strictly aerobic or strictly anaerobic conditions but require a "partial oxygen pressure." It will be interesting to compare Rosenow's findings with those of Poynton and Paine: if it should turn out that the bacterial origin of acute rheumatic fever is demonstrable, a most important step forward will have been made.

infectious disease, probably depending upon a primary infection in the throat with secondary invasion of the blood with the virus (virus-æmia) and metastatic joint involvement.

The tendency at present is to limit the use of the terms "rheumatism" and "rheumatic" to diseases due to this unknown virus which causes "acute rheumatic fever." This is why, today, the term "chronic rheumatism" is, perhaps, best reserved for a chronic arthropathy due to the virus which causes acute rheumatic fever. There may be some reason, as T. McCrae has emphasized, to doubt the existence of such a chronic arthropathy; some of the evidence available is rather against it, though a number of the best authorities on diseases of the joints believe that it does exist, and the matter is best considered as yet unsettled. It can scarcely be definitely decided until the etiological agent in acute rheumatic fever is determined and it is found out whether this is present or absent in the cases of supposed "chronic rheumatic arthritis."

DIFFERENTIATION OF THE CHRONIC ARTHROPATHIES ACCORDING TO THE PATHOLOGICAL ANATOMICAL CHANGES MET WITH IN THE JOINTS.⁸

If we now examine the attempts to classify the chronic arthropathies based upon pathological anatomical changes in the joints, we find that investigators have made their divisions according to two main principles:

1. The principle of considering the part of the joint involved (*site of the lesion*), and
2. The principle of considering the kind of morbid anatomical process concerned (*nature of the lesion*).

(*ad* 1) Thus according to the first principle, pathologists in coining names have classified joint diseases as follows:

- (a) Those involving a joint as a whole (for example, *pan-arthritis*).
- (b) Those involving predominantly the soft parts about a joint (for example, *peri-arthritis*, *peri-articulitis*, *arthromeningitis externa*).
- (c) Those involving predominantly the synovial membrane and its villi (for example, *synovitis* [*arthromeningitis*] *interna*, *arthritis villosa*).
- (d) Those involving predominantly the cartilages and bones of a joint (for example, *arthritis deformans* (Virchow); *osteoarthritis deformans*).

⁸ Excellent accounts of the anatomical changes can be found in the articles by Nichols in Keen's System of Surgery, Nicholson in the Cambridge report, Ziegler in his text-book, Schmidt in Aschoff's text-book, and Cornil and Ranvier in their *Histologie pathologique*.

An interesting example of the application of this first principle is discernible in the early descriptions of the chronic joint-diseases now known to be due to tuberculosis. The older authors separated them, according to the site of the lesion, into (1) those beginning in the soft parts (synovialis and periarticular tissues) and (2) those beginning in the ends of the bones entering into the formation of the joints. They called the former "white swelling" (*tumor albus*), and the latter "caries" (*arthrocace*). Billroth, thinking this distinction artificial, grouped both varieties under the term "fungous arthritis."

The sequels of joint-diseases have also been classified, in part at least, according to the site of the anatomical change; thus the distinction made between "true ankylosis" (*ankylosis vera*) and "false ankylosis" (*ankylosis spuria*) depends upon whether there is a union of the joint-surfaces themselves, as in the former instance (*ankylosis intracapsularis*), or, as in the latter, there is rigidity of the capsule (*ankylosis capsularis*), or of the periarticular soft parts (*ankylosis extracapsularis*).

(ad 2) Again, according to the second principle above mentioned, we might classify the chronic joint-diseases as follows:

- (a) Those depending upon abnormal processes in development—the "malformations" or "teratological arthropathies" (*A. teratologica*; *A. congenitalis*).
- (b) Those depending upon degenerative or metabolic processes (*A. chronica degenerativa*; *A. metabolica*), including, perhaps, (1) the atrophic arthropathies seen in tabes (*A. tabidorum*) and syringomyelia, and (2) the tophaceous deposits of gout (*A. urica*).
- (c) Those due to abnormal processes of circulatory or vasomotor origin (*A. chronica circulatoria*), including atherosclerotic arthropathies, the hemophilic arthropathies, and hydroids intermittens.
- (d) Those dependent upon defensive and reparative processes, viz., the chronic inflammatory arthropathies (*A. chronica inflammatoria*), including, in the sense of Lubarsch.
 - (da) The chronic alterative inflammations (*Arthritis chronica alterativa*) in which regressive changes predominate, though with them are associated less marked exudative and productive processes. Here would be included the "atrophic arthritis" of Goldthwaite and of Nathan.
 - (db) The chronic exudative inflammations (*Arthritis chronica exudativa*), including the round-celled infiltrations and the chronic purulent and ulcerative processes in the joints (gonorrhea, tuberculosis, etc.). Here would be classed also many cases of arthritis following the other infections, and, probably, also many of the cases described

as "rheumatoid arthritis," as "primary progressive polyarthritis," or as "arthritis nodosa" (Schuchardt) in their *early* stages (when there is effusion or periarticular swelling).

(*dc*) The chronic productive inflammations (*arthritis chronica productiva*) in which proliferative changes in the fibrous tissues, cartilage, or bone predominate. The process may represent (1) an end-stage of an acute or subacute arthritis, or of an exudative arthritis of insidious onset, slowly progressing, (2) an arthritis which has been "dry" and "productive" from the beginning (*arthritis sicca* = *arthrite sèche* of French writers), or (3) a so-called "specific inflammation" or "infectious granulomatous change." Under chronic productive arthritis two main anatomical groups may be distinguished, according as (*i*) the joint-capsules or (*ii*) the bones and cartilages are the site of the principal productive changes. When the productive inflammation affects chiefly (*i*) the joint capsules, it often leads to either shrinking or to relaxation of these capsules; the bones become rarefied and softened; and the cartilages undergo absorption. If along with these changes the cartilages and the bones show no marked tendency to proliferation, we have the condition so often observed in cases of "primary chronic progressive polyarthritis" (= *Polyarthritis destruens* of A. Hoffa); owing to the softening of the bones, they easily undergo plastic distortion from the pressure exerted on them by shortening capsules or by muscular contractions; the ends of the bones flatten out; if they can deviate sidewise, they do so, giving rise to characteristic subluxations; when lateral deviation is prevented by the ligamentous structures, as at the carpus, the bones are squeezed into one another, undergoing the change so graphically described by the Boston school of orthopedists as "telescoping of the bones," with shortening of the parts in the proximodistal diameter. When the finger-joints are affected, the shortening of the proximal or middle phalanges by this telescoping process may be very striking, especially in the x-ray plates. The fibrosis and shrinking of the capsules in the disease just described put it anatomically in the larger group known as "adhesive or ankylosing arthritis" (*A. chronica adhesiva*; *A. chronica ankylopoietica* (Ziegler). But by this term is usually meant a chronic productive inflammation, which leads not only to pericapsular fibrosis and to fibrosis of the synovial layer of the joint-capsule with partial or complete obliteration of the recesses of the joint-cavity, but also to

pannus-formation on the articular surfaces, followed by complete fibrous or bony union of the opposing surfaces (*ankylosis fibrosa*; *ankylosis ossea*). This anatomical type includes many of the chronic ankylosing inflammations of the joints which follow infections, among other forms, the so-called "rheumatismus fibrosus (Jaccoud), and the kind of "poker-spine" known as "ankylosing spondylitis" (*spondylitis ankylopoietica*), in which there is true ankylosis of the joint-surfaces of the articular processes of the vertebræ and of the costovertebral articulations, along with ossification of the longitudinal ligaments of the spine. When the productive inflammation affects predominantly (ii) the bones and cartilages, the result is a "deforming arthritis" (*arthritis deformans*) with exostoses, osteoporosis, osteosclerosis, fibrillation, and atrophy of cartilage, ecchondroses, sometimes combined with villous proliferation, "lipoma arborescens," etc. Such changes may occasionally be met with as the end-stage of an alterative or of an exudative inflammation of long standing (= "secondary arthritis deformans"), but they seem to appear much more often, and more characteristically, as a process *sui generis*, productive from the first, with marked lipping of bones at the edge of the articular surfaces (= *primary arthritis deformans* = *osteoarthritis deformans* = *hypertrophic osteoarthritis*). The "primary osteoarthritis deformans" may involve more than one joint, though even then it appears usually as an oligoarticular affection rather than as a general involvement of the joints. As subvarieties of it may be mentioned (1) "hypertrophic osteoarthritis of the spine" (*spondylitis deformans*), and (2) "senile osteoarthritis of the hip-joint" (*malum coxæ senile*), a monoarticular affection in which erosions of cartilage with exposure of bone are marked, hence sometimes called "dry ulcerative arthritis" (*arthritis ulcerosa sicca*); in this malady there is often less periostitic proliferation than in other forms of osteoarthritis. It is in the various types of deforming arthritis, especially, that "free bodies" (*corpora libera articulorum*) (of the hard variety) are prone to be found (*Gelenkmause* of the Germans; *corps étrangers* of the French). In the third group of the chronic productive inflammations of the joints may be placed (iii) the so-called "specific" chronic inflammations or "infectious granulomatous" inflammations of the joints (*arthritis chronica granulomatosa*), including the different forms of tuberculosis, syphilis, leprosy, actinomycosis, etc., of the joints, differentiable in part on morbid anatomical

changes (tubercle, gumma), but more easily when their causes are studied. In this group, particularly, the necessity of helping out anatomical classifications by distinctions based upon etiology was relatively early found to be pressing.

- (e) The chronic diseases of joints due to true tumor growth (*arthropathia neoplastica*) are rare. Primary sarcomas and endochondromas occasionally occur, but they are far less common than the proliferative and metaplastic processes of *arthritis deformans*, simulating (and often erroneously designated as) fibroma, enchondroma, or osteoma.

DIFFERENTIATION OF THE CHRONIC ARTHROPATHIES ACCORDING TO THE ETIOLOGICAL FACTORS KNOWN, OR PRESUMED, TO BE CONCERNED.

While conceptions based on pathological-anatomical changes have perhaps been dominant in the origin of names for the joint-diseases, we can also make out all through the terminology of the arthropathies the influence of etiological conceptions.

Phenomena accompanying diseases of the joints depend upon the "abnormal" alterations in the substances and energies of the parts; they are the "reactions" of the "system" to the "stimuli" which reach it. The structural changes involved in such reactions form the basis of the pathological-anatomical classifications, while the abnormal conditions determining the constitution of the system, the abnormal stimuli reaching the system, and the routes followed in reaching it, form the basis of etiological classifications.

The arrangement of substances and energies in a "joint-system" at any given time depends upon (1) the germ-plasm from which the individual has been derived, and (2) the influences, internal and external, which have acted (from the time of fertilization) upon the particular portions of the germ-plasm from which the joint-system came. In any broad consideration, therefore, of the causes of joint-disease such as is required if a differentiation of disease on etiological grounds is contemplated, the two factors of *heredity* and *environment* (internal and external) would have to be analyzed. That, in the chronic arthropathies, heredity in some instances is largely responsible, environment in some, every one will grant; to bring conviction on this point we have only to point to the gouty and the hemophilic arthropathies on the one hand, and to the traumatic and the infectious arthropathies on the other.

Knowledge regarding disease processes is, however, far too limited as yet to permit us to say how much a given "reaction"

is due to factors of heredity, how much to factors of environment, or, again, how much is due to "internal" causes and how much to "external." The "external" causes are, it is true, much better understood than the "internal." What we call "exciting" causes are very often external, while "predisposing" causes may be internal or external or both. Further, when dealing with a special "organ-system," like a "joint-system," and using the terms "external" and "internal" causes, we have to keep clearly in mind the fact that such terms may refer to the "organ-system" by itself or to the whole organism of which the "organ-system" is but a part. This point becomes especially important when in a given instance of polyarticular disease we ask first, Why are the joints diseased at all? and second, Why are some joints involved and others not?

When diseases of joints are named according to conceptions of etiology, the names sometimes refer to the mode of access of the pathological stimulus to a joint-system, for example, injury from the outside (= *traumatic arthropathy*), injury through the blood (= *hematogenous arthropathy*), injury through the lymph channels (= *lymphogenous arthropathy*), injury through the nerve paths (= *neurogenous arthropathy*)⁹

But, sometimes, names based on etiological conceptions refer rather to the particular variety of injury, that is, to the especial form of abnormal stimulus concerned; thus *physical* stimuli are concerned in traumatic arthritis, and, presumably, in the so-called "static" joint diseases (*statische Gelenkerkrankungen* of Preiser), *chemical* stimuli in the "toxic" arthropathies (for example, *arthralgia saturnina*), and *biological* stimuli in the "infectious" arthropathies due to bacterial invasion of the joints (*arthritis infectiosa*; *rhumatisme chronique infectieux* of Chauffard and Ramon).

And, in the third place, names suggesting etiological conceptions may refer neither to the mode of access of the noxa to the joint (*exposition* of the joint-system), nor to the particular variety of noxa concerned, but rather to some more or less vague predisposing causal factor (*disposition* of the joint-system or of the organism as a whole). Thus a predisposing *age* (as in *malum coxae senile*), or the predisposing conditions of *poverty*, involving a combination of under-nutrition, cold, moisture, and depressing psychic influences (as in *poor man's gout* and *arthritis pauperum*) may be reflected in the terminology.

To deal with all the etiological conceptions upon which differentiations of the chronic arthropathies are being based, would be

⁹ Distinctions might, perhaps, be made among the "neurogenous arthropathies." It may be that some are due to influences injurious to the joints acting directly through nerve-fibres, and that others arise in individuals suffering from neuropathy (tabes, syringomyelia); in the latter, there is room for discussion as to whether the injurious influences reach the joint directly through the nerves (perverted trophic influence) or through direct physical influences from the outside (trauma) as a result of loss of protective centripetal influences (anesthesias).

beyond the scope of this report, but two of the ideas merit especial comment, on account of their influence upon contemporary medical thought. I refer (1) to infection, and (2) to static influences.

The chronic arthropathies of infectious origin. Since septic processes have been carefully studied by bacteriological methods and their joint complications have been found to be toxic-infectious processes due to the arrival in the joint, by way of the blood-stream, of some of the bacteria causing the general sepsis, the idea of an infectious origin of arthropathies has proved to be an illuminating conception. By far the majority of acute, febrile, non-traumatic arthropathies are now believed to be infectious in nature. In many instances the bacteria have been grown in pure culture from the inflammatory exudate in the joint. As examples of bacteria thus found responsible, may be cited (1) the gonococcus (in *polyarthritis gonococcica* following gonorrheal infection of the urethra, or of the conjunctiva), (2) the pneumococcus (in *polyarthritis pneumococcica* complicating lobar pneumonia), (3) the streptococcus (in *polyarthritis streptococcica* complicating erysipelas, streptococcal angina, puerperal infection), (4) the staphylococcus (in *polyarthritis staphylococcica* as a part of general staphylococcus sepsis), and (5) the meningococcus (in *polyarthritis meningococcica* complicating epidemic cerebrospinal meningitis). Now, since these acute infectious (hematogenous) arthritides of definitely determined bacterial origin sometimes end neither in death nor in early recovery, but in a chronic process in the joints (for example, chronic gonococcal arthritis), the idea of an infectious origin for many of the chronic arthropathies has gained credence (Bannatyne, Charrin, Chauffard, Goldthwaite, Schüller). The notion was soon extended to various chronic arthropathies in which, despite the absence of demonstrated bacterial causation, the local processes in the joints and the state of the rest of the body (slight fever, slight leukocytosis, secondary anemia, enlargement of the lymph glands, slight foci of local infection elsewhere) make the assumption of a continuous (or occasionally recurring) bacteriemia of low grade with joint-deposition seem possible and plausible (Allchin, Baer, Cave, Goldthwaite). Under this heading come the severe forms of arthritis occurring in childhood (Still's disease).

At the present time, the term "infectious arthritis" is used in a very loose way. It has been made to refer to (1) the arthropathies in which bacteria have been actually demonstrated in the diseased joints, especially in the infectious granulomas (tuberculosis, lues, lepra) and in those complicating the septicemias, (2) the arthropathies which appear obviously as complications, or as sequels, of diseases believed to be infectious, no matter whether the causal agent is demonstrable in the joints or not (for example, acute rheumatism; arthritis after influenza), no matter whether the joint disease is supposed to be due to the same cause as the primary

disease or to a secondary invader¹⁰ (for example, arthritis after dysentery), no matter whether the germ of the primary disease is known or not (for example, arthropathies associated with or following scarlet fever, mumps, etc.), and no matter whether the assumed toxic infectious process affects the joints directly, or indirectly through the mediation of trophic nerves (according to the views of some regarding so-called atrophic arthritis and primary chronic progressive polyarthritis). Obviously, here, vagueness passes the permissible and a judicious restriction of the term "infectious arthropathy" seems desirable. Whether we should, with the rigid restrictionists, limit its use to arthropathies in which bacteria are actually demonstrable in the joints, or should extend it to include the arthropathies which may reasonably be supposed to be due to local bacterial deposition, though such deposition cannot yet be demonstrated, is open to discussion. We do not hesitate to regard scarlet fever and measles as acute infectious diseases, though their microbic origin still awaits demonstration, and, personally, I cannot help feeling it legitimate to designate as "infectious" the arthropathies like those of acute rheumatic fever, and those chronic types growing directly out of acute or subacute processes associated with fever, leukocytosis, and enlarged lymph glands. But, pending further investigations, it does seem desirable when differentiating the arthropathies on etiological grounds, carefully to distinguish (1) the demonstrably infectious from (2) the probably infectious, (3) the possibly infectious, and (4) the certainly non-infectious. We should also, when using the term "infectious," keep clearly in mind the difference between (a) an infection in a joint-system itself, and (b) an infection somewhere in the organism as a whole, with secondary non-infectious changes (toxic, nutritive, trophic) in a joint-system. I emphasize this point because of the great importance, in the chronic arthropathies, of minute foci of infection distant from the joints and of their removal as a therapeutic measure. Chronic inflammations of the paranasal sinuses (including the antrum of Highmore), chronic tonsillitis, chronic otitis media, pyorrhea alveolaris, alveolar abscess, chronic bronchitis, chronic ulcerative enteritis, chronic appendicitis, cholecystitis, chronic pyelitis, chronic cystitis, chronic urethritis, spermatoecystitis and prostatitis, chronic salpingitis, and chronic endometritis may be mentioned among the many possible foci whence influences injurious to the "joint-systems" of the body may emanate, and this without prejudice as to whether these influences are (1) metastatic infectious, (2) toxic, (3) neurotrophic, or (4) noxious in still other ways.

Much interest has been shown in the possibility of an infectious

¹⁰ It would seem that many of the cases described as Poncet's disease (*rhumatisme tuberculeux*) are really instances of infectious arthritis of unknown origin occurring in individuals suffering from tuberculosis, rather than metastatic tuberculous infections of the joints.

origin for the so-called "primary chronic progressive polyarthritis" or "rheumatoid arthritis" of Garrod. The mode of onset in certain cases, the course, and the x-ray changes have made many believe that this terrible disease is due to a chronic infectious process involving joint after joint. Though bacteria have from time to time been described in the joints, the findings of the observers are discordant. If the malady be a specific infectious disease the future will have to determine the microorganism responsible, the portal or portals of entry into the blood, and the important predisposing factors. The possibility that this disease may be due sometimes to one microorganism, sometimes to another, must also be kept in mind. For, though the clinical and pathological changes are so uniform that they suggest a single specific cause, our experience with meningitis, pleuritis, etc., has taught us to await actual knowledge before attempting to close a discussion.

The chronic arthropathies of static origin (Arthropathia chronica statica). Recently a view has been advanced by Preiser according to which the "arthritis deformans," in the sense of the pathologists, in both its primary form and its secondary form (*vide supra*), is due to abnormal static conditions in the body. Applying Albert's law of the static unity of the lower extremity—"the pelvis, thigh, leg, and foot form a static unit"—and extending the conception also to the upper extremity, Preiser maintains that a disturbance of a static unit is felt not only locally, but, also, usually in all the joints belonging to the unit. In a rachitic genu valgum, for example, in addition to the displacement at the knee, the position of the head of the femur in the acetabulum is abnormal, and the apposition of the articular surfaces in the ankle-joint is disturbed; in other words, a "pathological incongruence" of the joint surfaces throughout the whole "static unit" results. A "pathological incongruence," while especially common as the result of rickets, may also follow the muscular weakness and softening of bones in other enfeebling diseases (influenza, visceroptosis), with change in the direction of a limb in its long axis, or, indeed, with rotation around any one of the three stereometric axes. In such states, the joint structures are more exposed to trauma and the nutrition of the joints may suffer from compression of the bloodvessels and nerves supplying them. Gradually the important changes of "arthritis deformans" appear in the form of fibrillation of the articular cartilages, degeneration, and proliferation of villi, marginal osteophytic outgrowths, and subchondral cyst-formation. While "arthritis deformans" is most often met with in advanced life, cases of "juvenile arthritis deformans" of the hip have been described; according to the view mentioned, they are looked upon as secondary arthritis deformans due to a "pathological incongruence" following the healing of an infectious (tuberculous) coxitis

in childhood. Those who support this static origin of chronic deforming osteoarthritis look upon the formation of osteophytes as an effort at compensation for the "incongruence" of the joint. They also see a support to the doctrine in the beneficial effects obtained from orthopedic measures directed toward the correction of flatfoot, genu varum, genu valgum, coxa vara, etc., in cases of deforming arthritis.

DIFFERENTIATION OF THE CHRONIC ARTHROPATHIES ACCORDING TO THE X-RAY FINDINGS.

Undoubtedly the greatest aid of relatively recent origin in the differentiation of the arthropathies during life is that yielded by radiographic examination. If good plates are made, not only is the condition of the bones and the cartilages clearly revealed, but much also can be learned concerning the state of the soft parts surrounding the joints, the synovial membrane with its villi, and the recesses of the joint-cavity.¹¹ A good radiograph is a veritable autopsy *in vivo* of a joint-system. We can decide at once as to the presence or absence of (1) periarticular swelling, (2) luxations or subluxations, (3) pathological deviations, (4) narrowing of joint slits, (5) atrophy or destruction of cartilage, (6) erosion of subchondral bone on the articular surface, (7) rarefaction or condensation of bone due to increase or diminution of lime-salts (also osteoporosis and osteosclerosis), (8) distortions of bone evidently due to softening and pressure, (9) tophi, (10) cysts, (11) osteophytes and exostoses, (12) subperiosteal swellings, (13) fibrous or bony ankyloses, (14) calcified free bodies, (15) calcification or ossification of ligaments, and (16) lime-deposits in bursæ. One of the most striking features often to be met with in x-ray plates is the evidence of so-called "acute bone atrophy" (Sudeck, Hale White, Kienbock, Exner). While a certain amount of rarefaction may result from inactivity or immobility, the very marked examples of "acute bone atrophy" are thought by some to be due to reflex trophic influences; others feel sure that even the marked examples are due to disuse (F. H. Baetjer) or to local toxic influences.

With the aid of Dr. F. H. Baetjer, the actinographer to the Johns Hopkins Hospital, I have recently studied carefully the x-ray plates derived from the arthropathic patients in the medical clinic and compared them with the clinical findings, as tabulated for me by Dr. Helen Watson. In this study we have been impressed by several points, most of all by the fact that the x-ray findings and classifications based thereon accord closely with those of

¹¹ The recesses of the joint-cavity are exquisitely revealed in x-ray plates made after injections of the joints with oxygen-gas. In the knee-joint, especially, if there be any doubt as to the differentiation between osteo-arthritis deformans and adhesive arthritis, examination by this method may be decisive.

pathological anatomy. *In the x-ray findings we have to deal entirely with form-relations and the inferences which can be derived therefrom.* It is not surprising, therefore, if in the terms "hypertrophic arthritis" and "atrophic arthritis" of the radiographers we meet again the "arthritis deformans" on the one hand, and on the other the "alterative arthritis," "adhesive arthritis," and "ankylopoietic arthritis" of the pathological anatomists.

Aside from gout, the neurogenic arthropathies, and possibly tuberculous and luetic arthritis, in which the x-ray plates are sometimes characteristic, the radiologist can rarely from the x-ray alone speak with any certainty as regards etiology. Again, as to predicting to which clinical group a given case belongs by inspection of the radiogram, the actinographer can often say that his "hypertrophic arthritis," with its non-obiterated joint-cavity, its condensation of bone, its large exostoses, and its marginal lippling, must belong clinically to (1) the benign osteo-arthritis deformans of advanced life (= primary *A. deformans*), to (2) an end-stage of an infectious or traumatic arthritis (= secondary arthritis deformans), or to (3) a neuropathic arthropathy; and he may suspect that his "atrophic arthritis" is clinically probably either (1) a primary chronic progressive polyarthritis (polyarthritis destruens) or (2) an arthritis secondary to some (other) infectious process. Further than this he is disinclined, and I think properly disinclined, to go. Finding how frequently disappearance of the joint slits, atrophy of cartilages, softening and distortion of bones with telescoping appear in the plates which he is told have come from patients suffering from "infectious arthritis," an actinographer's tendency may be to group all cases exhibiting these changes under the heading "infectious arthritis." This inference may turn out to be justifiable, though it is, as yet, hypothetical. For distinguishing, by x-ray examinations, the different kinds of infection (gonococcal, streptococcal, etc.), with the exception, perhaps, of the luetic and tuberculous types, adequate criteria are lacking. In an x-ray report, therefore, we should discriminate sharply between (1) the objective morphological findings reported, and (2) any interpretative impressions regarding probable etiology or probably clinical type. A report from an x-ray laboratory which gives merely a diagnosis couched in etiological terms may be very misleading to clinicians; in the team-work of a great hospital, therefore, the radiographers on making their reports should be encouraged to describe objectively the abnormal form-relations found, and to give only anatomical diagnoses; or, if they, through long experience in the correlation of x-ray findings with clinical phenomena, feel themselves justified in drawing clinical or etiological inferences, they will be most helpful if they will definitely designate the latter as such in an appendix to the actual x-ray report.

What has been said above refers to the x -ray study of the joints in general. But the actinographer and the clinician must be familiar with the x -ray findings peculiar to each joint-system. The technique of radiography is rapidly undergoing great improvement. The precise position of the parts at the time of exposure may be determining as to whether an abnormality present in the joint becomes visible, or not, in a plate. As examples may be mentioned (1) the difficulty of revealing slight bone changes in the shoulder-joint (P. Ewald, 1911), and (2) the difficulty (until Schlayer in 1906 showed how in the lumbar region to project the joint slits into the intervertebral spaces in the plate) of studying the changes in the joints between the articular processes of adjacent vertebræ in ankylosing spondylitis.

Reports on individual joints in the most different diseases are now available, but in a very scattered bibliography; it would be most helpful if we could have an epitome of this material brought together in a single volume.

THE PRINCIPAL CHRONIC ARTHROPATHIES ARRANGED IN CLINICAL GROUPS.

Though many attempts have been made systematically to arrange the chronic arthropathies in clinical groups, none of them has proved wholly satisfactory or attained to universal acceptance. While clinical observation has taught us that certain well-defined types are met with over and over again, presenting such characteristic appearances and running such constant courses that they are deserving of treatment as separate clinical entities, when we are actually confronted by an individual case which deviates somewhat from the more "typical" forms, it may be extremely hard to place it, with entire satisfaction, in any one of the classes set up. Attempts at clinical classification are further complicated by the fact that one and the same clinical type has often been described under different names, and, worse still, and most systematic writers complain of it, each of these names may have been used also for other, wholly different, types. The failure of the terminologies based upon anatomical, etiological, and clinical conceptions to coincide with one another has been made, in the preceding sections of this report, sufficiently clear. The same difficulty of harmonizing classifications made for these three different purposes has been met with, often enough, in other domains, for example, in pneumonia, in osteomyelitis, in conjunctivitis, in angina. An agreement among these different modes of classification could only be expected, as Lubarsch has emphasized, if the course of the pathological phenomena depended exclusively on the factors starting the process, and if the organism were not able to react in different ways to the same stimulus. But since

the course and nature of disease are dependent upon many circumstances other than the external and internal stimuli concerned, and the cells possess only a limited number of modes of reaction, it is not possible that the clinical and anatomical phenomena of diseases can be satisfactorily rubricated on the basis of the different noxæ giving rise to them. In other words, we can never expect more than a partial coincidence of clinical, anatomical, and etiological groupings.

In modern clinical classifications, however, we feel justified in utilizing not only the anamnesis and the results of our general physical, chemical, and biological studies of the patient, but also (1) pathological-anatomical conceptions insofar as the x-ray findings and our physical examinations will permit us to value them, and (2) etiological conceptions insofar as they also can be valued through the anamnesis and through special chemical and bacteriological tests in given cases. The terminologies used for clinical purposes, therefore, are no longer based simply upon external appearances and the mere course of the disease, but must often reflect also anatomical and etiological considerations based upon a correlation of clinical experience with anatomical finding and demonstrated causal relationships. There can scarcely be objection to this as long as we clinically do not attempt to draw other than really justifiable anatomical and etiological inferences.

As a tentative classification of the principal diseases usually grouped under the designation chronic arthritis, the following rubrics would seem to be, at present, most useful:

- I. The true gouty arthropathies (*A. chronica urica*).
- II. The arthropathies of severe nervous disease (*A. tabidorum*; *A. syringomyelica*).
- III. The (primary) hypertrophic osteoarthropathies (osteoarthritis hypertrophicans or osteoarthritis deformans), a relatively benign affection.¹²
- IV. The secondary chronic arthropathies, following various infections (*A. luetica*, *A. tuberculosa*, *A. chronica gonorrhoeica*, *A. chronica rheumatica*, if it exist, etc.), and those following small foci of infection (microorganisms often unknown) in various parts of the body.

V. The so-called (primary) chronic progressive polyarthritis—of all arthropathies the most malign.

In relation to the above five headings mention must be made of several special conditions; namely:

- (a) The villous arthritis of Goldthwaite.
- (b) The chronic arthropathies of the spine.
- (c) Still's disease.

¹² This is not to be confused with the "osteoarthropathie hypertrophiante pneumique" of Marie or "pseudoacromegaly," in which there is slow thickening of the bone beneath the periosteum—the "toxigenic osteoperiostitis ossificans" of Sternberg.

- (d) Heberden's nodes.
- (e) Bouchard's comptodactylie.
- (f) Subcutaneous fibroid nodules.

Confronted with a single case of chronic arthropathy it is often convenient to consider groups I to V above mentioned in serial sequence.

ad I. The *true chronic gouty arthropathy* is usually easy to recognize, at any rate in the typical cases. The heredity, the acute exacerbations, especially as nocturnal attacks, the presence of tophi, the sites of predilection, the increased amount of uric acid in the blood (Garrod, Magnus-Levy), and the deficient purin tolerance (method of v. Noorden and Schliep, 1905), suffice for the diagnosis. In atypical cases there may, however, be some difficulty in distinguishing the disease from atrophic or infectious forms of arthritis. The x-ray findings in a gouty joint are sometimes distinctive (spherical foci in the bone substance near the joint, or often in the form of a semicircular defect of the articular surface of a bone with sharp, punched-out margins; if such a lesion be present in a joint of one foot there is often a similar lesion in the same joint of the other foot).

ad II. The *neuropathic arthropathies* are easily ruled out if, in addition to the examination of the joints, a thorough neurological investigation be made (tests of sensibility, knee kicks, pupils, etc.). Moreover, the sudden onset, the marked enlargement of a single joint, and the absence of severe pain, are characteristic. Astounding changes are made visible by the x-rays; bizarre, monstrous hypertrophic lesions predominate; besides excrescences upon the bone and huge calcified free bodies, calcified masses are usually visible in the extra-capsular tissues; some regressive (atrophic or absorptive) changes are also present and there is usually extreme disintegration of the joint.

ad III. The (*primary*) *hypertrophic osteoarthropathy* (osteoarthritis [osteoarthropathia] hypertrophicans or deformans) is usually easily recognizable. Though most often met with in advanced life, the same or a similar malady may occur in youth, especially after slight trauma. One joint is chiefly affected, or several joints (usually only a few) may be involved. This mono-articular, or oligo-articular, distribution is in marked contrast with the more general polyarticular distribution of Groups IV and V. The large proximal joints of the extremities are most often involved (hips, shoulders, knees). There is an absence of the steady progression characteristic of Group V. Both sexes are affected, males predominatingly. The general health may be but little disturbed. The disease does not lead to true ankylosis, though the joint-

movements may be somewhat limited through interlocking of exostoses. On palpation, lipping of the bone at the edge of the cartilage may be sometimes made out. Free bodies are common. In radiograms, the joint-slits are often well preserved though the cartilage may be eroded, accounting for the grating which may be palpable on movement of the joint; the joint-slits do not entirely disappear, as in Group V and often in Group IV. As the joint-cavity is not obliterated, if oxygen be injected (method of Werndorff and Robinson) the capsule unfolds well, showing the absence of extensive adhesions and of shrinking. The presence of extensive osteophytic outgrowths, or of marked marginal lipping in the x-ray plates, especially when the clinical symptoms have been slight, is characteristic. Static disturbances, leading to pathological incongruence of the articular surfaces, and a history of trauma are common in these cases. The disease is often asymmetrical. Among the monoarticular forms, the so-called *malum coxæ senile* is included. One of the spinal arthropathies (*spondylitis deformans*) appears to belong in Group III (*vide infra*).

ad IV. In considering the possibility of a *chronic arthropathy secondary to some infectious process* it is well to think first of the chronic arthropathies due to infectious granulomatous processes (tuberculosis, lues, lepra, etc.). Here the white swelling (*tumor albus*) of Wiseman, a suppurating fistula, the anamnesis, the presence or absence of lesions elsewhere in the body due to the primary disease, the study of x-ray plates (destructive processes in tuberculosis, sub-periosteal swellings, regular or irregular in outline, in lues), the Wassermann reaction, and the tuberculin tests may help to clear up the diagnosis. After lues and tuberculosis have been excluded, the anamnesis may be gone into very carefully with reference to a history of a preceding acute infection, either of the joints themselves or of other parts of the body. One tries to determine whether or not the chronic arthropathy has followed a true acute articular rheumatism or one of the so-called acute infectious pseudo-rheumatisms (*vide supra*). It is clear from our examination of many of the cases recorded in the bibliography as "chronic rheumatic arthritis" following acute articular rheumatism, that the authors were in reality not dealing with a chronic arthritis following this affection (in the narrower sense) at all, but with a chronic arthritis following some one of the various other forms of acute infectious arthritis. Cultures from the blood, from the joint-fluid or from a regional lymph gland, complement-deviation tests, tests for bacteriolysins, agglutinins, etc., may occasionally be of help. This study may be followed by a systematic physical examination

in which the various possible primary foci of infection, mentioned in a preceding paragraph under infectious arthritis, are sought for. The search for intracellular Gram-negative diplococci in "milkings" from the prostate and urethra in the male, or from Bartholin's glands, the urethra, and the secretions from the cervix uteri in the female, and a thorough examination of the nose and of the paranasal sinuses, utilizing the methods of transillumination and of x-ray examination of the sinuses, should here form a part of the regular routine. The presence or absence of pyorrhea alveolaris, of antrum disease, of abscesses at the roots of the teeth (x-ray), of chronic tonsillar infection (palatine or pharyngeal), and of chronic otitis media, should be determined. If the case be seen in the later stages, a marked asymmetry of the joints affected, an absence of steady progression, or the complete ankylosis of single joints, may speak for Group IV rather than for Group V.

ad V. If the case does not clearly belong to one of the first four groups it is most important, from the standpoint of prognosis, to decide whether or not it really belongs to Group V, the so-called *primary chronic (progressive) polyarthritis*.¹³

Clinically, primary chronic progressive polyarthritis (Group V) may appear as either one of two sub-varieties. In both of these, the involvement is outspokenly polyarticular, the small distal joints of the fingers, toes, wrists, ankles, usually being involved first. Later, the knees and elbows may become involved; the hips and shoulders frequently escape. These small joints become involved symmetrically. The jaw joint and the sternoclavicular joint are not infrequently affected, and, curiously enough, usually asymmetrically. Some of the cases of ankylosing spondylitis (*vide infra*) belong to category V.

¹³ The term "primary" in Group V and the term "secondary" in Group IV are used in a sense similar to the terms "primary" and "secondary" in connection with the anemias. We speak of a "primary anemia" when we mean an anemia of the Addisonian or Biermer type, not secondary to any well-known cause of anemia, though we realize that it must be secondary to some cause. Similarly, the "primary chronic polyarthritis" may not be obviously secondary to any acute primary infection elsewhere in the body. If it be an infectious disease, however, the bacteria or their toxins must reach the joints by way of the blood, and the bacteriemia and the polyarthritis are then "secondary" to some primary focus of infection. Until the etiology is determined definitely, however, there would seem to be no objection to the use of the word "primary" in this way. It seems likely that the word "primary" was applied to this disease in the first place in a different sense, meaning that the disease was chronic from the beginning (the *rhumatisme chronique d'emblée* of French writers); it seems now that it may, especially in childhood and adolescence, sometimes begin subacutely or even acutely with fever and sweat. The term "primary chronic progressive polyarthritis" is rather unwieldy on account of its length. There is much to be said in favor of A. E. Garrod's suggestion to use "rheumatoid arthritis" instead; the objection to this lies in the fact that "rheumatoid arthritis" has been used to comprise both this type and Group III, while Gerhardt referred to the infectious pseudo-rheumatisms preceding the chronic cases of Group IV as "rheumatoids." If there could be a general agreement to limit the term "rheumatoid" to V, the expression would be a convenient one for clinical use.

In one sub-variety (A) the disease may begin either insidiously or with an acute, or subacute, stage, with fever; in both forms of onset a striking feature is the periarticular swelling. Each joint of the proximal row of the joints of the fingers (with the exception of the thumb) often presents a spindle-shaped or fusiform appearance and feels elastic when compressed between the thumb and forefinger of the examiner. Most of the small joints in the distal parts of all four extremities may become affected in serial sequence. It is often impossible in the early stages to decide whether we are dealing with a true chronic progressive polyarthritis of Group V or with one of the serious maladies of Group IV.

In the second sub-variety (B), most often met with in women near the menopause, the onset may be very insidious. The patients complain first of formication, of chilly feelings, and of slight stiffness of the metacarpophalangeal and interphalangeal joints (except those of the thumb). Muscular atrophy quickly appears, especially of the interossei. Contractures gradually develop. The disease spreads to a large number of the more distal joints in all four extremities. The fingers become deflected ulnarward. The hands may present the "flexion-type" or the "extension-type" of Charcot, or the "straight" type, but these do not represent essential differences and are unimportant for classification. On x-ray examination the joint-slits are found to have disappeared, owing to atrophy of cartilage, the bones are softened, and may have undergone distortion or telescoping, and they are usually markedly atrophic—so-called "atrophic arthritis" of Goldthwaite (*vide supra*).

The sub-variety A is sometimes called the *exudative type*; it is the "periarticular type of arthritis deformans" (in part) of T. McCrae, and corresponds to the "nodosities" of Haygarth, the *rhumatisme nouveau* of Trousseau, the "arthritis nodosa" of Schuchardt, and the "chronic infectious arthritis" (in part) of Goldthwaite.

The sub-variety B is the so-called *dry form*, and corresponds to the "atrophic arthritis" of Goldthwaite, the "atrophic type of arthritis deformans" of T. McCrae, and the *arthrite sèche* (in part) of French writers.

The sub-variety A can certainly be simulated by chronic gonorrheal polyarthritis; x-ray plates will not distinguish between them. In lues hereditaria tarda an arthropathy similar to sub-variety A is sometimes seen, but it should not be difficult to exclude it (Hutchinsonian teeth, keratitis, positive Wassermann, luetic changes in x-ray plate at epiphyseal line).

The absence of endocardial and pericardial changes in "primary chronic progressive polyarthritis" is striking when contrasted with the findings in acute rheumatic fever, the acute pseudo-rheumatisms, and in the chronic infectious arthritides.

It cannot be too strongly emphasized that sub-variety B is often (some think always) an end-stage of a condition beginning as sub-variety A. It ought to be acknowledged, too, that it is *possible* that later on Group V will not be considered separately as a disease *sui generis*, but will be placed in Group IV; in other words, it may be that the clinical appearances described as V may follow upon a variety of infections. For the present, the weight of evidence seems to me to favor the view that V is really an independent disease of unknown though unitary etiology (probably infectious).

A few words must now be said concerning the various special joint conditions mentioned above and their relation to the five main groups.

(a) *The Chronic Villous Arthritis of Goldthwaite.* This form of "dry joint" is believed by Goldthwaite not to be a general disease at all but a local process entirely, with no tendency to progression, characterized by an absence of general symptoms, by crepitation or creaking of the joint on motion, with varying degrees of pain and tenderness on movement. It is most commonly met with in the knee as the result of flatfoot. This type appears to be one of the "static arthropathies" of Preiser. It probably corresponds in Hoffa and Wollenberg's classification to "chronic irritative arthritis." It seems likely that it may follow the action of causes of different kinds.

(b) *The Arthropathies of the Spine.* The subject is difficult to deal with in a few words. The most important point to emphasize is, it seems to me, the fact that the joints and bones of the spine are subject to diseases precisely in the same way as the other joints of the body. We meet in the spine with (1) the gouty, (2) the neuropathic (tabetic), (3) the hypertrophic osteoarthritic, (4) the secondary chronic infectious, and (5) the primary chronic progressive forms. Anatomically, aside from traumas, the neuropathic arthropathies and the infectious arthritides of the spine (tuberculosis, lues, gonorrhea, typhoid, etc.), which usually affect the spine locally rather than throughout its whole extent, two main processes seem to occur in the vertebral column: (1) a hypertrophic osteoarthritis of the spine (*spondylitis deformans*) and (2) a chronic ankylosing arthropathy of the spine (*spondylitis chronica ankylopoietica*).

In hypertrophic osteoarthritis of the spine (*spondylitis deformans*) the process seems to begin in the intervertebral disks; there are marked exostoses on the bodies of the vertebra and, especially, "lippling" of the vertebral bodies at the edge of the intervertebral disks, often with a few clasp-like formations extending from vertebra to vertebra, but never so extensively as in the ankylosing forms. The small joints between the articular processes never undergo intracapsular ankylosis in this disease, though

motion may be limited by exostoses. The nerve roots may be compressed. The disease occurs chiefly in advanced life. It almost never causes complete rigidity of the thorax.

In *spondylitis chronica ankylopoietica*, the disease begins in the small joints of the articular processes and quickly leads to ankylosis; the costovertebral articulations are often involved also. The ligaments of the spine sometimes become ossified, but many of the bony bridges or clasps uniting the vertebræ may be independent of the ligaments. Of this chronic ankylosing spondylitis, two clinical forms have been described: (1) the "Marie-Strümpell subtype" beginning below and extending upward, described by Marie as *spondylose rhizomélique*, on account of the simultaneous involvement of the articulations of the vertebral column and the proximal joints of the extremities (hips, shoulders); and (2) the "Bechterew subtype" with outspoken kyphosis of the upper thoracic spine, the process beginning above and extending downward.¹⁴ Later studies (Fraenkel, Simmonds, Janssen, Anschütz, Plesch) have shown that all sorts of transitions exist between the Bechterew type and the Strümpell-Marie type; these two subtypes do not represent anatomically separable processes in the spine. Rigidity of the spine is easily recognizable clinically. Pains in the spine, radiating into the trunk or the extremities, stiffness gradually extending to all movements of the spine, with a tendency to kyphosis, are characteristic phenomena.

The differential diagnosis between spondylitis deformans and the ankylosing variety is, in most cases, easily made. If the breathing be wholly abdominal owing to ankylosis of the costovertebral articulations or to the general approximation of the origin and insertion of the accessory respiratory muscles from kyphosis or from stiffness of midthoracic spine, or if the disease occur in young persons, under forty years, it is almost certainly chronic ankylosing spondylitis. The spine is more uniformly involved throughout its whole length in the ankylosing type than in spondylitis deformans. Radiograms are decisive in most cases. As to early cases, in spondylitis deformans the bone changes may be marked and the clinical symptoms slight, while in the ankylosing spondylitis severe clinical symptoms may precede demonstrable bone and joint changes by a year or longer.

(c) *Still's Disease*. This disease, a chronic arthritis of childhood, described by G. F. Still (1897), probably represents neither a clinical nor an etiological unity. In Still's disease we appear sometimes to deal with a secondary chronic infectious arthritis (Group IV) and sometimes with a primary chronic progressive polyarthritis (Group V). The presence of a large spleen; large

¹⁴ A few of the cases described clinically as Bechterew's type turn out on x-ray examination to be spondylitis deformans.

lymph-glands, leukoeytosis, and secondary anemia are strongly suggestive of chronic infection.

(d) *Heberden's Nodes*. These nodes are due to exeresenees on the base of the terminal phalanges of the fingers. They are easily reecognizable on inspection, on palpation, and in the x-ray. In my experience they ooeur most often in assoeiation with chronic hypertrophie osteoarthropathies, though they are sometimes seen in gout, and they sometimes ooeur as an isolated phenomenon, not assoeiated with arthritis of the other joints. In the x-ray the adjaeent joint may be but slightly affected, or, in some eases, the joint may show ehanges like those in primary chronic progressive polyarthritis. Heberden's nodes cannot, therefore, be said to be pathognomonic of any one form of chronic arthropathy; indeed they seem to ooeur in eonnection with several different forms, and by themselves. It would seem probable that Heberden's nodes do not represent even a morphologieal unity. They appear sometimes to be true exostoses (in hypertrophie osteoarthritis), sometimes to be projeetions due to softening and flattening of the base of the terminal phalanx (in infeetious and in chronic progressive arthritis), and, finally, sometimes to be nodules due to gouty ehanges in the bones. Dr. W. S. Baer tells me that even on palpation varieties of Heberden's nodes are distinguishable; certainly in radiograms a variety of structures can be made out in the different types of eases.

(e) *Bouehard's Comptodactylie*. Bouehard has deseribed fusiform swellings of the proximal finger-joints as an aeecompaniment of dilatation of the stomach; they are said to disappear when the stomach lesion is eured. Pribram has seen one sueh ease. I have not observed this relationship. The relation of chronic arthritic affeetions to various disturbances of the digestive traet has been emphasized by Coutaret and also by Goldthwaite (in viseeroptosis).

(f) *Subcutaneous Fibroid Nodules*. These little bodies attaeched to the tendons and faseiæ (Meynet, Barlow and Warner, T. B. Futeher, Hawthorne) may ooeur in almost any form of chronic arthritis. They were at one time supposed to be pathognomonic of true "rheumatic" affeetions. They are not to be confused with the *nodosités cutanées éphémères* of Fereol.

In bringing this report to a close I would reëmphasize certain points, namely: (1) The constant recurrence of well-characterized clinical types in the experience of observers in all countries; (2) the astonishing accuracy and vitality of the names that have been used for definite purposes; (3) the unfortunate confusion which has arisen largely through trying to use names introduced for a specific purpose for entirely different purposes, and especially through the efforts to make clinical, anatomical, and etiological classifications coincide; (4) the gratifying progress in differen-

tiation thus far made in a group of diseases formerly supposed to be one disease; and (5) the prospect of still more satisfactory differentiation to follow advances in etiological knowledge when they can be made. It is to be hoped that the discussion may go far toward clarifying our ideas of the chronic arthropathies; may it also spur us on to researches which will lead us, gradually, still further along the path out of vagueness toward definiteness!

SOME CAUSES OF DISAPPOINTMENT IN OPERATIONS ON BRAIN TUMOR.¹

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THE discussion on brain tumor introduced by Bruns and Tooth² at the recent International Medical Congress, called forth some discouraging statements. Bruns said that about 30 out of 100 brain tumors are so situated that a radical operation may be advised; the localization is accurate and the tumor is accessible. He believed we may expect surgical success in 3 to 4 per cent. of all brain tumors. Tooth studied the records of 500 cases of brain tumor at the National Hospital, obtained during the years 1902 to 1911 inclusive. Of these about half came to operation. He thinks a high mortality is inevitable, but we must not be dismayed by it. We can reduce the mortality by judicious choice of cases for operation and by selection of the operation best suited for individual cases. The immediate dangers common to all growths, all situations, and apparently all operations, are shock, collapse, and respiratory and cardiac failure.

Many causes of disappointment will occur to anyone familiar with operations for brain tumor. The best known are incorrect diagnosis; infiltrating character, large size, and inaccessible situation of the tumor; mistakes in technique and impaired general vitality. Others equally important may be mentioned, but I desire in this communication to speak of the enlargement of the brain caused by tumor, the distortion of the brain especially from tumor in the posterior cranial fossa, and the acute swelling of the brain, probably an important element in the production of hernia cerebri, conditions which usually may be avoided by sufficiently early operation and proper technique.

¹ Read by invitation at a meeting of the New York Neurological Society with the Section on Neurology and Psychiatry of the Academy of Medicine, November 11, 1913. Lantern slides were used to illustrate the paper, but only a few are represented here.

² Proceedings of the XVII International Medical Congress.

It is important to remember that when tumor develops in the brain and exists for a long time alteration of the brain structure even in regions remote from the tumor may occur. Failure to take into consideration this alteration may lead to disappointment when operation does not produce the desired result. A tumor may be removed in whole or in part and yet symptoms may persist if a large part of the brain has undergone structural change. Late operation, and most radical operations for brain tumor are late from necessity, is likely at the best to afford recovery with defect, and this defect is dependent in a measure on the altered condition of the brain caused by tumor.

Increase of intracranial pressure is believed to be a cause of many of the general symptoms occurring with brain tumor, and it would seem from the writings of certain authors that the increase of pressure is attributed directly to the tumor and varies with the size of the tumor. There is a condition resulting from tumor to which little attention has been paid, and which is as important if not more so than the size of the tumor, viz., enlargement of the brain. This hyperplasia is not directly proportional to the size of the tumor, it may be of moderate degree, with a large tumor or sufficient to cause much enlargement of one cerebral hemisphere where the tumor is small. The hyperplasia may be the result of irritation either from pressure or possibly from some substance elaborated by the tumor, and is caused by overgrowth of neuroglia tissue. The condition is not unknown in medical literature, although little is said concerning it. Oppenheim remarks that the irritation which the tumor causes to the brain may lead to general swelling and increase in the size of the brain, upon which structural change, as proliferation of the neuroglia, follows. The disturbance of the normal relation of cranial capacity to weight of brain leads to functional alteration.

This hyperplasia of the brain may occur with almost any variety of tumor, and is not confined to glioma. It should not be confused with enlargement from glioma tissue, for it has not the appearance microscopically of tumor. It should not be confused with the acute brain swelling of Reichardt.³

Tumor external to the brain apparently does not lead to hyperplasia unless it causes much pressure upon the brain. In four cases of tumor of the cerebello-pontine angle I examined in which little pressure upon the brain was produced, no hyperplasia developed, but in another case in which a tumor of this angle caused considerable pressure upon the occipital lobe hyperplasia of the cerebral hemisphere of the same side was pronounced.

According to Reichardt, disease of the posterior parts of the

³ Zeitschrift für die gesamte Neurologie und Psychiatrie, Referate und Ergebnisse, 1911, iii, 1.

brain in man may cause considerable swelling of the whole brain, and in this way choked disk may be produced. Sudden death may occur from tumor of the pons or medulla oblongata when choked disk has not been present, and this may occur from acute terminal brain swelling.

Reichardt believes the brain swelling as understood by him is not detectable with the microscope. The swelling may be confined to one cerebral hemisphere or to part of a hemisphere. It is probable that the swelling is caused by increased capacity of the brain tissue for fluid. The fluid enters into intimate combination with the brain tissue and is not recognizable as fluid, and the brain may even appear dry.

Increase in size of the brain may be from various causes: from increase of free fluid in the tissue spaces, from increase of histological elements, from hyperemia, etc., but this is not the brain swelling of Reichardt. The true brain hypertrophy has no relation to the brain swelling, as the latter can appear and disappear rapidly.

The enlargement of a cerebral hemisphere, in which a tumor is situated, by irritation and proliferation of the neuroglia, does not seem to come under the designation of brain swelling as understood by Reichardt.

This hyperplasia of tissue near a tumor is not confined to the animal kingdom, but exists also in the vegetable kingdom. In the illustrations used in a lecture delivered before the Pathological Society of Philadelphia, by Edwin F. Smith, the tissue appeared to me to be proliferated about the tumor strands in plants much as the brain tissue becomes proliferated near a tumor.

The sudden fatal termination that occurs in some cases of tumor probably is a result of this enlargement of the brain, and of interference by the general increase of intracranial pressure with the important functions of the medulla oblongata. In other cases sudden death occurs from hemorrhage or injury of vital parts of the brain by the tumor, the pressing of the medulla oblongata against the edge of the foramen magnum, etc. In my experience, hemorrhage is not the most common cause of sudden death in brain tumor, although I have known it repeatedly to be diagnosed when sudden death occurred.

If the brain be examined by a neuroglia stain there will be found in some instances an overgrowth of neuroglia even in areas at a considerable distance from the tumor. Such increased density of tissue must interfere with the function of nerve fibers, and many of the remote symptoms of tumor probably are from this cause as well as from disturbance of function in associated tracts (diaschisis). The picture given by Rosenthal⁴ in his article on pseudotumor,

⁴ Zeitschrift für die gesamte Neurologie und Psychiatrie, 1911, vii, No. 2, 170.

representing neuroglia proliferation, is much like certain sections from one of my specimens (Fig. 1), but I have not been able to demonstrate proliferation of the neuroglia in all cases. A neuroglia proliferation of moderate intensity is not easily shown even with a neuroglia stain. While I believe that in many cases the permanent enlargement of the brain in association with brain tumor is the result of proliferation of the neuroglia, in whatever way it may be produced, I wish to emphasize the fact that this enlargement of one cerebral hemisphere even if produced in some other way than by proliferation of neuroglia is likely to cause symptoms in addition to those caused by the tumor.

Some of the remote symptoms may be produced by changes in the nerve cells from the tumor. Redlich⁵ found in some cases of

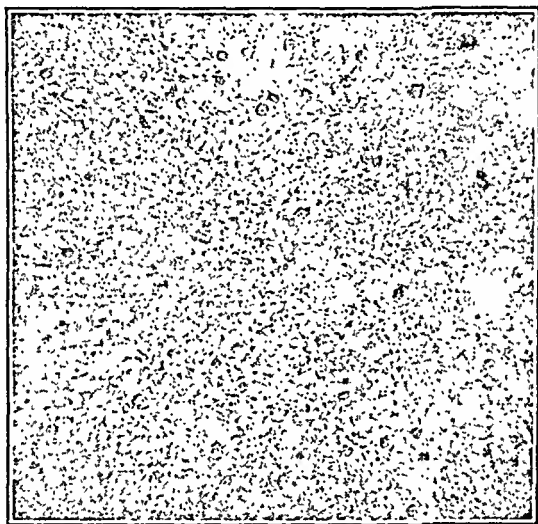


FIG. 1.—Photograph of a section from the centrum semiovale below a small tumor of the parietal lobe. The whole cerebral hemisphere of this side was much enlarged. The neuroglia is shown proliferated in irregular masses. (Mallory's neuroglia stain.)

brain tumor with mental symptoms alteration of the nerve cells and nerve fibers in pieces taken from different parts of the brain, but he could not find the changes in the glia spoken of by Reichardt, and no increase in neuroglia fibers except near the tumor. The changes Redlich found resembled those of senility, and did not satisfactorily explain the mental symptoms associated occasionally with brain tumor.

It may be that hyperplasia of the brain is an important cause of impairment of mentality in some cases of brain tumor. I have

⁵ Obersteiner's Arbeiten, vol. xv. part 1,

known large endotheliomas to exist without any impairment of intellectual power, and in such cases one finds that the tumor has grown slowly, has caused much atrophy of the underlying brain, but may not have led to hyperplasia of a large part of the brain. Some of my cases of enlargement of a cerebral hemisphere presented symptoms which it would be difficult to attribute to the tumor directly. In one, a glioma (449) (Fig. 2) of the pons caused considerable

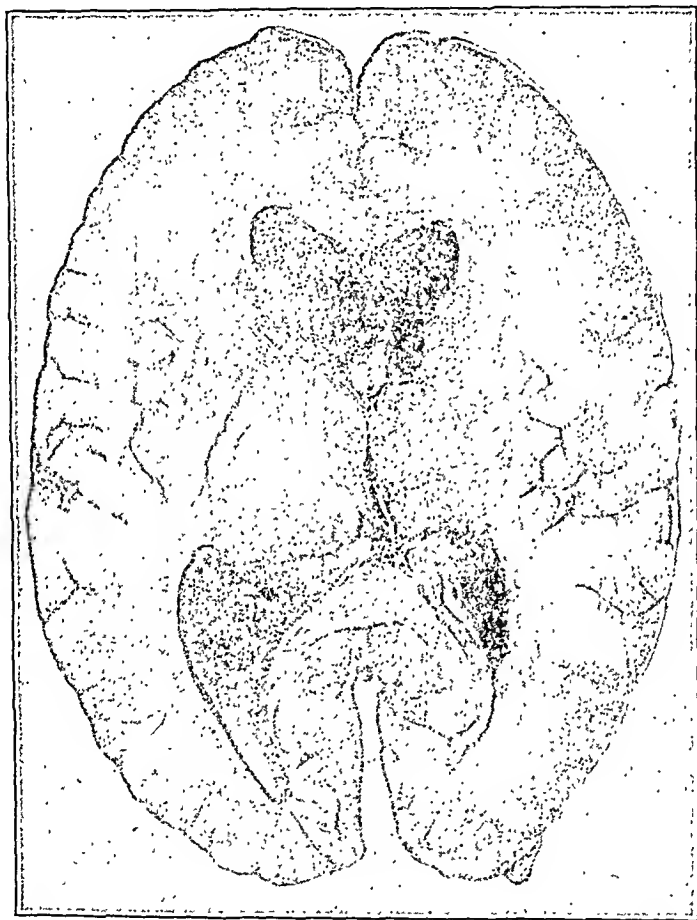


FIG. 2.—Enlargement of one cerebral hemisphere caused by a glioma of the pons.

enlargement of one cerebral hemisphere. The patient presented some symptoms which it would be difficult to explain entirely from a pontine lesion. She was hungry all the time and childish. Excessive hunger as a sign of brain lesion I have observed several times.

In another (422) (Fig. 3), a glioma was found in the region posterior to the right optic thalamus. The portion of the right hemisphere in front of the tumor was considerably enlarged. The speech was slurring, and tests words were pronounced with difficulty. The

memory was poor and the man was easily confused. He acted queerly, attempted to disrobe in public, and did not know how to put on his clothing. He had been alcoholic, so that the effects of alcohol cannot be eliminated, yet I believe that some of his symptoms may have been caused by the hyperplasia.

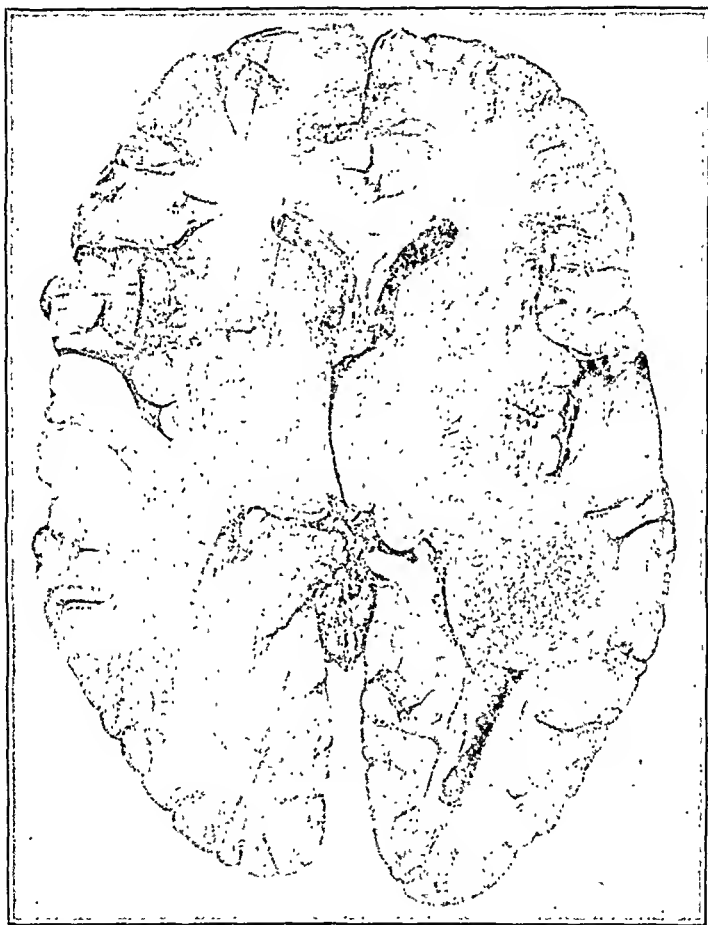


FIG. 3.—Glioma in the region posterior to the right optic thalamus. The same side in front of the tumor is much enlarged.

Another case was interesting in that death occurred very suddenly; the tumor was small, but the whole cerebral hemisphere of the same side was much enlarged. In still another (Keesler), sudden death occurred and a small tumor was found in the left lateral lobe of the cerebellum, and another, also small was found in the right motor region of the cerebrum, but no hemorrhage was revealed.

It is important to state that the enlargement in all these cases was not from distortion as a result of pressure from a tumor. The

parts preserved their relative positions, but were considerably enlarged.

Indeed one of the greatest enlargements of the brain I have observed was from a small tumor of the parietal lobe measuring in a transverse section of the brain 2×3 cm. The enlargement of the cerebral hemisphere on the side of the tumor was as great as that represented in Fig. 2. Fig. 1 represents a section from this case.



FIG. 4.—Tumor of the occipital lobe. The cerebral hemisphere containing the tumor is much enlarged.

Distortion of certain parts of the brain is a grave complication of tumor. I have already discussed this in a recent paper in *Brain*. The displacement of the cerebellum and occipital lobes complicates operation, as sudden relief of pressure probably has injurious effects on parts distorted gradually. The medulla oblongata may

be so distorted that with the upper cervical cord it forms a half circle. This occurred in a brain from a patient in my service at the Philadelphia General Hospital (Fig. 5). Cranial nerves in the region of the medulla oblongata are liable to be stretched gradually by such distortion, and the effect of this stretching on the pneumogastric may be serious. The distortion in this case was explained by the pressure from a large cyst occupying the greater part of

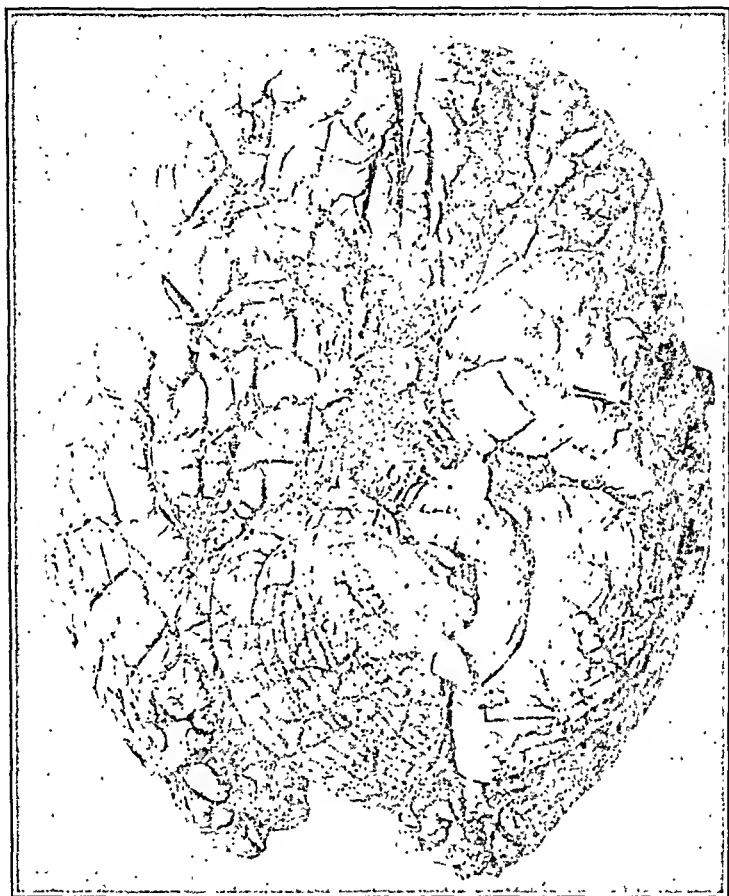


FIG. 5.—Atrophy of the left lobe of the cerebellum and distortion of the medulla oblongata, caused by a large cyst of the left cerebral hemisphere. Displacement of the medulla oblongata of this degree is likely to affect the cranial nerves connected with it.

the left cerebral hemisphere, communicating with the lateral ventricle of the same side, and causing atrophy by pressure of the left cerebellar hemisphere. The cyst evidently was from occlusion of the anterior cerebral artery, as its extent corresponded to the distribution of this artery as given by Beever. One might well consider whether it would not be desirable to delay the removal of a large tumor causing much displacement of the brain, after it had been revealed at operation, until a later operation had

given time for the brain to readjust itself in some degree to the changes of pressure following the opening of the dura.

Hernia cerebri is a serious complication of operation for brain tumor. Where it results from decompression it has been supposed to be indicative of the degree of intracranial pressure and to show to what extent intracranial pressure has been relieved. This view is not entirely correct. Intense intracranial pressure possibly may be more liable to cause hernia than intracranial pressure that is more nearly normal, and yet much hernia may develop where there has been no decided increase of intracranial pressure. A large hernia occurred in one of my cases in which a thrombus of the inferior petrosal sinus of long duration had caused atrophy of the adjoining pons, the intracranial pressure could not have been greatly increased, nevertheless a large hernia developed. It seems probable that in such cases acute swelling of the brain in the sense of Reichardt may be responsible for the hernia.

A hernia may cause pressure against the edges of the opening in the skull, with occlusion of vessels and softening of the parts of the brain implicated in the hernia, causing in this way hemiplegia and other grave symptoms.

I am indebted to Dr. A. J. Smith for the photographs.

THE MECHANISM OF THE CIRCULATORY FAILURE IN DIPHTHERIA.

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In the course of acute infections it is well known that the patient may die with symptoms somewhat like those of surgical shock. The blood-pressure falls, the pulse becomes weak and small, the skin is pale or cyanotic about the nose and ears, sweating and vomiting ensue, and with shallow respiration and general collapse, the heart stops beating.

The discussion as to the mechanism of this disturbance is so well known that only the briefest *résumé* need be given here. It had long been thought from clinical observations that the affection might be one of the vasomotor apparatus rather than the heart itself, and Romberg, Pässler, Brühns, and Müller attempted to prove this in the case of diphtheria, pneumococcus, and pyocyaneus infections by experimental studies. In these studies they relied upon certain methods which aimed to demonstrate that the heart would regain its activity if the failure of the vasomotor apparatus

were overcome in some way, and that those things which ordinarily caused vasomotor reactions were ineffectual. Thus they found that the mechanical expression of the blood from the splanchnic veins into the heart would restore for a time the aortic pressure, and with that the coronary blood-supply, and thus the nutrition and activity of the heart. The same could be produced by compressing the aorta. Barium chloride still caused the vessels to contract, but sensory stimuli had lost their effect. They, therefore, concluded that the circulatory failure was not due primarily to injury of the heart, but rather to the paralysis of vasomotor centres in the brain, which, causing a lowering of arterial resistance, quickly affected the heart through the diminished coronary supply to the heart wall. Romberg especially pointed out the fact that if the heart were at fault all these tests should fail.

Then Stejskal criticized their methods, showing that abdominal massage could increase arterial pressure even in a dead animal, and that its effects are very transient. He believed that the heart itself is directly injured, and fails on that account. Gottlieb supported this view to some extent, believing that the withdrawal of blood from the coronary circulation need not kill the heart so rapidly, since a heart may be kept for hours after the animal's death and then revived by perfusion. He therefore concluded that death probably was due to respiratory stoppage, with subsequent failure of the heart, due to its injury by the poison.

Rolly and Pässler later reviewed the subject, and seem to admit the force of Stejskal's objections as to the abdominal massage; and though they maintain the idea that the injury to the heart is through malnutrition, they state that it becomes very susceptible to other injuries. Other writers, whose papers are referred to below, lean to one or the other view or accept the idea that both vasomotor paralysis with its consequences and direct injury to the heart wall occur.

In the course of a study of the mechanical conditions present in aortic insufficiency, a plan was devised by which the influence of the vasomotors might be almost entirely eliminated and the work of the heart studied by itself.¹ This plan consisted in simply dividing the aorta near its root and connecting it with a long rubber tube, ending in a curved glass outlet, which could be elevated to any height upon a graduated upright pillar. The aortic pressure could in this way be set at any point according to the height to which the heart must drive the blood against the force of gravity. The blood which escaped fell into a cistern and returned through another long tube to the distal part of the aorta. Of course, by applying this arrangement to an animal in the collapsed condition which follows poisoning with the diphtheria toxin, the injurious effects of paralysis

¹ W. G. MacCallum, Johns Hopkins Hosp., Bull., 1911, xxii, 197.

of the vasomotors would be removed at once, and if the theory of the Leipzig school be correct, the heart should return to its normal activity and the animal continue to live.

The following protocols will illustrate the results of this experiment:

Dog 1.—Weight, 8.9 kg. April 25, 1911, 1 A.M. The dog was given 1 c.c. diphtheria toxin intravenously. At 11 A.M. the animal was found lying sick in the cage. Carotid pressure was taken at 11.30. Chest was opened and the circulation arranged as described, the outlet being set at 130 cm., which was the carotid pressure before the operation. The heart beat well for two hours, after which there appeared great edema of the lungs, and the heart dilated and stopped. All of the organs were found to be edematous, and showed numerous ecchymoses. The heart beat regularly throughout, and the output was well maintained.

Dog 6.—Weight, 6.6 kg. May 3, 1911, 12.45 A.M. The dog was given 0.75 c.c. diphtheria toxin intravenously. At 1 P.M. the carotid pressure was taken, the aorta cut, and external circulation arranged. This was finished at 1.20 P.M., and the heart beat well until 3.10 P.M., when there was extreme edema of the lungs and of other organs. In the heart, which was otherwise grossly normal, there were many hemorrhages. Here as in the first case the heart continued active for two hours.

Dog 7.—Weight, 10.3 kg. May 5, 1911, 12.30 A.M. The dog was given 2 c.c. diphtheria toxin intravenously. At 12 noon the dog was apathetic and drowsy. At 2 P.M. it vomited and appeared very weak. Artificial or external circulation arranged at 2.40 P.M. and the heart beat at a pressure of 110 cm. blood until 5.35 P.M. At times the heart began to collapse and beat with great excursions, driving out relatively little blood. One dose of digitalin and strychnine was given, which restored it to its normal beat. During the latter part of the three hours there were violent general convulsions.

Dog 13.—Weight, 6 kg. April 2, 1913. The dog was given 3 c.c. diphtheria toxin intravenously at 10.30 A.M. It was found very sick at 4 P.M., and at 4.45 P.M. the external circulation was arranged, after which the heart beat quite well until 7.20, when the supply of blood failed and the experiment was stopped. There was some irregularity in the action of the heart, but on the whole it beat strongly for two hours and thirty-five minutes.

In order to have a good control observation, two dogs of the same size were given the same dose at the same time. It was intended to show that with the aid of the maintenance of arterial pressure one could be kept alive long after the other had died.

Dog 14 A, weight 10,560, female, and Dog 14 B, weight 10,900, male. Each dog was given 4 c.c. diphtheria toxin intravenously at 8 A.M., April 3, 1913. Both dogs had vomited and were depressed

and weak at 5 P.M. Dog A was found lying stretched out stiffly and not breathing. Heart not beating. Artificial respiration was begun. Carotid pressure was very low. It was attempted to establish the external circulation, but through an accident the dog died. By this time, 5.35 P.M., Dog B was almost dead, and lay inert. Reflexes were gone, the eyes rolled about, and there were convulsive twitchings. External circulation was established at 5.45 P.M. and tracings of the heart-beat were taken until 8.35 P.M., a period of two hours and thirty-five minutes when the heart stopped, apparently only because it finally became necessary to use blood which had been kept several days.

Dogs 15 A and B, weighing respectively 11 and 10.3 kg., were given 4 c.c. diphtheria toxin at 8 A.M., April 8, 1913. At 3.55 P.M. both dogs were almost dead, lying quite apathetic with complete loss of reflexes and occasional convulsions. Dog A, whose blood pressure as taken from the carotid was very low, about 60 cm. of blood, was arranged with the external circulation and the outflow tube set at 85 cm. The heart-beat improved at once and continued from 3.30 to 4.40 P.M. In the meanwhile Dog B died at 3.20 P.M. The character of the pulse of Dog A, as seen in the tracing, varied spontaneously being rapid and strong at times and producing an abundant outflow, while at other times there was a slower collapsing beat, which propelled relatively little blood to the outflow. After one hour and ten minutes it became distended during a convulsion, and could not be made to beat again. It seemed that in this case at least the heart itself had been injured by the poison.

For comparison normal dogs were subjected to the same operation as shown in the following protocols:

Dog 2.—Weight, 6.9 kg. Anesthetized with chloretone April 28, 1911. External circulation complete at 3.30 P.M.; pressure set at 130 cm. blood, which equals about 100 mm. mercury. At 4.45 P.M. there was much oozing from cut tissues, and the heart became distended. Pressure lowered to 53 cm. and heart beat again. Some edema of lungs and of other tissues. Given a dose of digitalin, after which heart beat well until 6.30 P.M., when the dog was killed.

Dog 5.—Weight, 9.9 kg. Anesthetized with ether May 2, 1911. The external circulation was arranged through one intercostal space at 3.20 P.M., and the outflow tube was set at 130 cm. of blood. The heart beat well until 6.20, when the dog was killed.

The actual output per minute of each of these hearts cannot be accurately determined from the curves produced by this method, because much of the blood circulates through the head and forelimbs, but since the records were all made in the same way, it will give some idea of the character of the heart's work after diphtheria poisoning to compare the output from the artificial aorta with that in the case of the normal dogs.

Dog 7 (Diphtheria).—Weight, 10.3 kg. Outlet was set at 110 cm.

Operation at	2.40 P.M.			
	3.30 "	100 c.c.	were delivered in 26 seconds.	
	4.00 "	100 c.c.	"	28 "
	4.30 "	100 c.c.	"	32 "
	4.35 "	100 c.c.	"	30 "

Dog 1 (Diphtheria).—Weight, 8.9 kg. Outlet was set at 130 cm.

Operation at	11.30 P.M.			
	12.00 M.	100 c.c.	were delivered in 18 seconds.	
	12.30 A.M.	100 c.c.	"	19 "
	1.00 "	100 c.c.	"	19 "
	1.30 "	100 c.c.	"	18 "

Dog 2 (Normal).—Weight, 6.9 kg. Outlet was set at 130 cm.

Operation at	3.30 P.M.			
	3.50 "	100 c.c.	were delivered in 21 seconds.	
	4.30 "	100 c.c.	"	20½ "
	5.45 "	100 c.c.	"	34 "

Dog 5 (Normal).—Weight, 9.9 kg. Outlet at 130 cm.

Operation at	3.00 P.M.			
	3.45 "	100 c.c.	were delivered in 35 seconds.	
	4.30 "	100 c.c.	"	29 "
	5.00 "	100 c.c.	"	30 "
	5.30 "	100 c.c.	"	29 "

From these it will be seen that the actual work of the diphtheria hearts was at least as good as that of the normal hearts.

It is probable that if the conditions were absolutely perfect and the exposure, use of defibrinated blood, etc., avoidable, it would be possible to keep a normal heart driving the external circulation for a longer time than three hours. It is probable, too, that even under the present circumstances a normal heart treated in the way the hearts of the poisoned animals were treated would beat a little longer and a little more steadily than they. But the difference is so slight that, while it seems probable from such spontaneous irregularities as occurred in the case of Dog 15 A, that the heart itself was injured by a large dose of toxin, it was clear enough that it was still able to carry on the circulation for two or three hours against a high pressure, a thing which is vastly different from mere beating in a perfusion apparatus.

It might be objected that the use of fresh blood would restore the heart by washing away the toxin, but in all these experiments the blood of the animal itself was returned to the circulation and was merely diluted. At any rate, Decroly and Ronnse showed that diphtheria toxin injected into the blood stream disappears completely after four to seven minutes, so that the injury is probably determined in some early part of the latent period. Rolly in his

experiments found that washing out an isolated heart with fresh blood had no effect in postponing the death of the heart, and apparently this was true. But while Rolly was unable to revive a poisoned heart, it proved to be not impossible, as the following protocols show.

DOG 16.—May 13, 1911. Isolated heart from normal dog perfused with Ringer's solution beat for two and a half hours at a rate of about 103. The drops of diphtheria toxin injected into the circulating fluid caused an immediate increase in rate to 200 after which the heart continued to beat for two hours longer at a rate of about 150.

DOG 17.—May 24, 1911. Isolated heart from normal dog perfused and was beating for one hour at a rate of 98. At 12.25 P.M. 1 c.c. of diphtheria toxin was added to perfusion fluid. This was followed by a marked stimulation of force and rate which rose to 112. The heart continued to beat until 3.30 P.M., when after a period of dissociation of auricular and ventricular beats it stopped.

DOG 18.—May 25, 1911. Weight, 5.7 kg. The dog was given 1 c.c. toxin intravenously at 11.10 A.M. At 6 P.M. the carotid pressure was low. At 10.30 A.M. the dog was extremely ill, and died at 10.55 A.M. The heart was found to have stopped beating. It was removed from the body and perfused with Ringer's solution, upon which it began to beat at 11.10 A.M., and continued to beat well for one hour and ten minutes.

DOG 19.—May 25, 1911. Weight, 5.9 kg. The dog was given 1 c.c. diphtheria toxin at 11.30 A.M. At 5.45 P.M. it was killed with ether and the heart excised and perfused with Ringer's solution. From 6.45 to 10.55 P.M. the heart beat strongly and regularly at a rate of about 90 to 110.

DOG 20.—May 25, 1911. Weight, 6.8 kg. Given 1 c.c. diphtheria toxin at 11.45 P.M. At 1 P.M. the next day the dog was nearly dead. It was killed at 1.35 P.M. and the heart perfused. The rate was somewhat irregular, varying from 44 up to 110, but for the greater part of the next two hours it beat strongly at about 62, stopping at 4.50 P.M.

DOG 21.—May 28, 1911. Weight, 7.8 kg. Given 2 c.c. of diphtheria toxin intravenously at 9.45 P.M. At 11 A.M. the next morning the dog was found dead, although alive and apparently fairly well a few minutes before. The heart was excised, but could not be started in perfusion apparatus until 11.50. At first there was fibrillation, but this was stopped by injection of potassium chloride, after which it beat somewhat irregularly until 2.15 P.M., a period of two hours and twenty-five minutes.

DOG 22.—May 30, 1911. Weight, 8.7 kg. Given 2 c.c. diphtheria toxin at 11 P.M. The next day at noon the dog died; the splanchnic vessels were much dilated. The heart was perfused at 12.15 P.M. and beat fairly well for three hours and forty

minutes, becoming edematous at last. For most of the time the rate was 96 to 100, but several times a spontaneous heart-block occurred, with a 1 to 2 rhythm, which each time suddenly changed back to the 1 to 1 rhythm.

DOG 23.—May 30, 1911. Weight, 8.2 kg. Given 1.5 c.c. diphtheria toxin at 11 P.M. The next day at 3.15 P.M. the dog was evidently dying. It was killed with ether and the heart excised and perfused. Perfusion began at 4 P.M., and the heart beat with varying rate until 7.20, a period of three hours and twenty minutes.

DOG 24.—June 1, 1911. Weight, 7 kg. Given 2 c.c. diphtheria toxin at midnight. At 11 A.M. the next day the dog was *in extremis*. The carotid pressure was very low. Etherized, and the heart was excised and perfused. It beat slowly from 11.20 to 2.25 P.M., about three hours, at a rate of about 52.

DOG 25.—June 2, 1911. Weight, 7.2 kg. Given 2 c.c. diphtheria toxin at midnight. At 1.15 P.M. the next day dog was very sick. Alcohol by stomach-tube had no effect upon the blood pressure, which sank until the dog's death at 2 P.M. At 2.10 P.M. the heart was perfused and beat normally at a rate of about 94 for three hours and thirty minutes, stopping at 5.40 P.M.

DOG 26.—June 3, 1911. Weight, 8.9 kg. Given 2 c.c. diphtheria toxin at 11.15 P.M. The next morning, at 9.30 the dog was found dead but not cold. Rigor was beginning. At 9.45 A.M. the excised heart was perfused and beat until 10.40 A.M. at the rate of about 100, rather feebly and irregularly.

In all these hearts the beat was rather feeble as compared with that of the perfused normal heart, and fibrillation seemed likely to occur. The note reads: "There is no comparison between the perfused normal heart and the diphtheria hearts, all of which are feeble and apt to go into fibrillation." Nevertheless, although one may receive the impression that the hearts from the poisoned animals are rather weak and apt to be irregular, it is clear that they continue to beat for several hours after they have shown every sign of failure in the body of the dying animal, if only the pressure of nutritive fluid be maintained in the coronary arteries. Indeed, the animal may be allowed to die, and an hour after its death the heart can be revived and will beat for a long time. All of this seems to show fairly well that the death which occurs in the height of an attack of diphtheria is not exclusively the result of direct injury to the heart, although that may play some part in the process.

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 Hoffmann. *Deutsch. med. Woch.*, 1912, xxxviii, 1865.
 Röhmer. *Zeitsch. f. exp. Path. u. Therap.*, 1912, xi, 426; *Jahrb. f. Kinderh.*, 1912, N. F. lxxvi, 391.

BLEEDING IN TYPHOID FEVER.

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It is generally recognized that the occurrence of hemorrhage in the course of typhoid fever is a serious matter, especially when it appears late in the disease. The degree of seriousness of this complication, however, has been differently estimated by writers, and one finds Trousseau and Graves constantly quoted as declaring that it was not an unfavorable event and sometimes even of advantage, while Murchison, Dieulafoy,¹ and others state that it is a bad omen and not even of transient benefit. Thus, on the one hand, Leibermeister² writes: "If at the end of the third or fourth week a large intestinal hemorrhage appears, it may occur that the marked fall of temperature with it will have a favorable influence upon the enteric phenomena present, recovery steadily advancing from that time on. These are the cases that have led competent observers (Graves, Trousseau) to maintain that intestinal hemorrhages are by no means unfavorable in enteric fever, but are rather of favorable prognostic import." On the other hand, Murchison wrote: "Although I have seen patients recover after a profuse hemorrhage, I have never seen the slightest benefit from it."³

It is admitted by every writer that the temperature often tends to fall after a hemorrhage, but most state that along with this lessening in the temperature there is a rise in the rate of the pulse. Thus, for example, Curschmann⁴ says: "In those cases in which the patient does not die during the first copious hemorrhage the clinical picture becomes alarmingly altered. The skin acquires a waxy

¹ Text-book of Medicine (translation), ii, 1626.

² Modern Clinical Methods in Infectious Diseases, p. 30; The Physiology of Blood-letting, *British Med. Jour.*, 1910, i, 104.

³ Sir Thomas Watson, Principles and Practice of Medicine, ii, 881.

⁴ Typhoid and Typhus Fevers, Nothnagel's Encyclopedia of Practical Medicine, p. 223.

pallor, there is relaxation of the features, the pulse becomes small and shows greatly increased frequency, lividity and coldness of the extremities and possibly syncope appear. With the rapid increase in the pulse frequency there is generally associated a rapid reduction in the bodily temperature. The curve may be observed to decline from 40° or 41° C. to far below the normal—to 35° C. and below—in a few hours. This characteristic intersection of the pulse and temperature curves is of grave prognosis.” He adds later, “Quite rarely I have seen the pulse-frequency fall parallel with the temperature curve—a condition that is without doubt to be considered as a favorable prognostic sign.” Again, T. McCrae,⁵ in speaking of hemorrhage in typhoid fever, says: “The temperature usually falls, and the drop may be as much as 10° and to below normal. Still, even a sharp hemorrhage may have no effect on the temperature. The pulse-rate rises, and with it the quality alters. At first somewhat bounding, later it becomes small and somewhat running.” He also says later: “That results of hemorrhage are very various, and there is no doubt that some patients do seem to be benefited. These are usually robust and but slightly toxic. The temperature curve may be lower, the pulse not increased in rate or even decreased, and the whole character of the attack milder.” One can easily realize that if the hemorrhage be very profuse a state of shock will ensue, with a marked fall in the temperature and rise in the rate of the pulse, along with all the other signs of an acute and profound anemia; but the rule seems to be, certainly in our series, that the temperature and pulse-rate fall together, with, as will be shown, a frequent improvement in the general condition of the sufferer.

It is difficult to believe that two such keen observers as Trousseau and Graves could have meant that bleeding in typhoid fever was not a serious thing, and probably Flagge was right when he wrote,⁶ “Probably the real basis of their opinion was the fact that a good many patients recover from it, or, in other words, that it was not so often directly fatal as might have been anticipated.” Certainly any statistical study of the disease makes it evident that the cases which have had hemorrhages have a much higher death rate than have others not so complicated. Thus in studying the last 1591 cases of typhoid fever treated in the Toronto General Hospital it appears that the mortality was 8.67 per cent. over all, but that the death-rate among those reported as having had one or more hemorrhages was 37 per cent. This latter figure is almost the same as occurred in Cruschmann’s series at Leipsic, which was 38 per cent.,⁷ while in Strümpell’s forty-five cases of hemorrhage in typhoid fever it was 42.2 per cent. In our series, if we exclude the cases

⁵ Osler’s Modern Medicine, i, 127.

⁶ J. Hilton Fagge, Principles and Practice of Medicine, i, 179 and 180.

⁷ Osler’s Modern Medicine, p. 127.

that had bleeding, we find that the mortality of the remaining 1464 cases was only 6.3 per cent.

The question here arises as to why enteric fever complicated with hemorrhage should have such a higher death-rate. The ill-effects of bleeding may be due (1) to the actual loss of blood, which may be directly fatal (as it was in eight out of Strümpell's nineteen deaths in typhoid complicated with hemorrhage), or the anemia may so weaken the patient as to lay him open to other complication, or (2) the bleeding may denote perforation, and in any case is usually significant of a severe infection. If it were not for these two classes of dangers, which are more or less imminent in hemorrhagic cases, the loss of blood, if of moderate amount, might be welcome. Many writers, for example Liebermeister and McCrac, not to mention Trousseau and Graves, have remarked how often patients seem to improve after moderate hemorrhages, and if it were not for the dangers looming up of the bleeding becoming uncontrollable or being a precursor of perforation, probably most physicians would be pleased rather than otherwise with the at least temporary benefit which so often accrues.

The appended twelve charts are taken from among the cases of intestinal hemorrhage (with one exception where the bleeding was through venesection) that occurred in our series at the Toronto General Hospital, and they show how the bleeding was followed by a more or less marked fall not only in the temperature but also in the pulse rate. They are perhaps the best examples, but most of the other one hundred and fifteen charts of cases with bleeding showed more or less of the same thing. They do not, of course, show the improvement in the general condition that was so often noted, but a perusal of the epitomes of the histories will make this evident. The notes of progress are exactly as they were made at the time by members of the staff and the house physicians. It will be noted that the improvement in the temperature and pulse curves, while often transient, in some cases may last for days and may even usher in convalescence. It is impossible in the face of such evidence to agree with Fagge when he says: "According to Liebermeister, hemorrhage also diminishes the pulse, and is often attended by a marked amelioration of the cerebral symptoms. But all these effects are transitory, for by the end of twenty-four hours the fever is as high or higher than before the hemorrhage." Or with Murchison, who wrote: "I have seen patients recover from profuse hemorrhages. I have never seen the slightest benefit from it."

It is difficult to explain how the good effects that may follow a hemorrhage come about. There is no doubt, however, but that it produces a profound effect upon the whole bodily economy. Thus bleeding has been shown to bring about an increase in the flow to urine;⁸ to greatly increase the intake of oxygen, with pro-

⁸ Potochi, *Revue Pratique d'Obstetrique et de Gynecologie*, January 20, 1911, No. 1, p. 28.

portionate raising of tissue-oxidation.⁹ It hastens the coagulation time of the blood more than does any other single agent with which we are acquainted.¹⁰ Roux and Vaillard showed in 1893 that it produced a rapid increase in the antibodies contained in the blood, and Dreyer and Schroeder, of Copenhagen, about four years ago, demonstrated that it increases the specific antibodies in typhoid and paratyphoid, both in experimental animals and in man. H. Whitehead¹¹ fully confirmed this two years ago in a study of typhoid complicated by hemorrhage, in which the agglutinating power of the blood was enormously raised by the bleeding. Further, in toxic conditions, such as uremia and other less-defined states, states, where there is high blood pressure, bleeding appears to in some way lessen the toxemia, and possibly in typhoid it may have some similar effect.

Finally, Whitehead, in his paper two years ago, suggested that the good effects of hemorrhage in typhoid fever might be attained and the evil ones (associated with intestinal hemorrhage) avoided by the timely use of venesection in those cases which are not doing well on account of severe infection and toxemia, and with this suggestion I heartily concur. Of course, in the days when venesection was considered to be a panacea for almost all ailments, cases of typhoid fever must have been bled, but it is impossible to get at any reliable data as to the results, as at that date typhoid fever was not differentiated from other cases of continued fever. Even Marshall Hall, who is considered to be the great opponent of bleeding, and who is given the credit of having brought about the almost complete abandonment of this time-honored method of treatment, states that in severe and eruptive fevers¹² from six to fourteen ounces of blood should be removed, so that it is not likely that cases of typhoid fever escaped.

So far only one case can be shown in our series (Case VII), but the sequence of the venesection was there most marked. Theoretically the method appears to be indicated in severe cases and if the removal of blood by venesection be a moderate one, say of six to fourteen ounces, as was recommended by Marshall Hall, it can do no harm and may possibly be productive of great good.

EPITOME OF CASES.

CASE 1 (Not yet filed).—Female, aged twenty-two years. Admitted October 1, 1911. Duration of illness, about two weeks. Was dull and drowsy; flushed.

⁹ Beaumont Small, *Reference Handbook of the Medical Sciences*, ii, 71.

¹⁰ Rudolf and Cole, *The Coagulation Time of the Blood in Various Diseases*, *AMER. JOUR. MED. SCI.*, October, 1911.

¹¹ *Intestinal Hemorrhage in Typhoid Fever*, *Lancet*, 1911, ii, 1067.

¹² Marshall Hall, *The Cyclopedia of Practical Medicine*, 1833, quoted by D'Arcy Power, *Practitioner*, 1909.

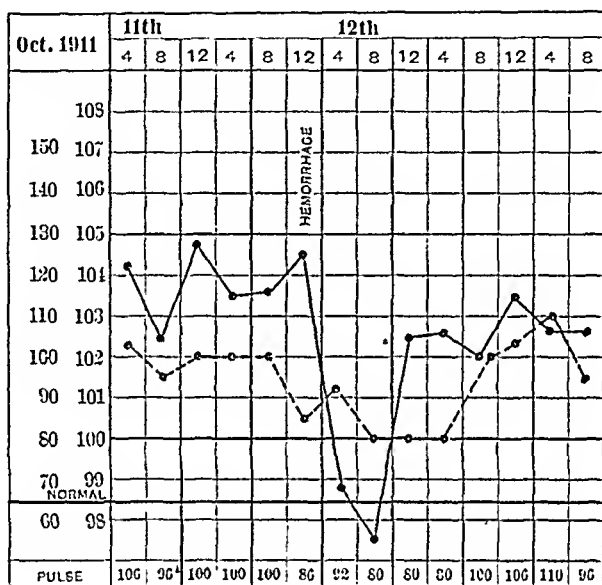
October 7. Vomited a great deal, and was dull and very toxic.

October 12. Very dull and toxic. Vomited twice. At 5.30 A.M. there was a profuse hemorrhage from bowel.

October 13. Brighter. Pulse, 92. Temperature, 98.6. Systolic blood pressure, 72; diastolic, 45.

October 19. Brighter. Toxemia not so marked. Temperature, 102.4°; pulse, 92; respiration, 22.

October 31. Quiet; sleeping well. No vomiting since October 12. Steadily improved, and was discharged well on January 21, 1912.



CASE I

CASE II (Vol. xxxix, Case 6088).—Male, aged thirty-five years. Admitted October 4, 1909. Duration of illness, about two weeks. Was in fairly good condition. Abdomen not distended; pulse very dicrotic.

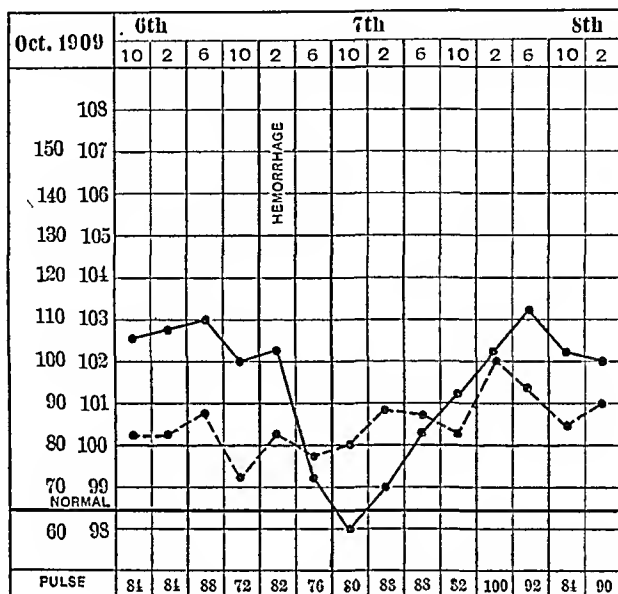
October 6. Chilly and free sweats. Lips dry. Tongue clean and red. Later in the day was drowsy and had severe headache and abdominal distress.

October 7. In early morning and again just before noon the patient complained of chilly feelings, and sweated. Was quite restless, and had severe abdominal pain, with no rigidity or tenderness. Some nausea. Bowel movement at noon showed small amount of dark blood. Half an hour later a large amount of blood. Pulse not changed. An hour later a third hemorrhage—very large. No change in pulse until then, when it became rapid, and he had a general faint feeling, blanched and hands clammy, and half an hour later had a profuse perspiration. At midnight the pulse-rate was not changed; temperature, 99°.

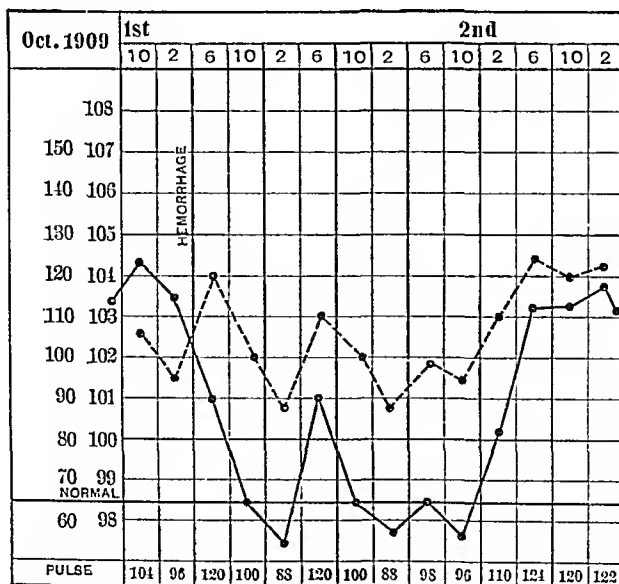
October 8. Slight hemorrhage at 9 A.M. This recurred slightly for two days. Pulse-rate not altered for the worse.

October 11. General condition satisfactory. Temperature running at a satisfactory height.

November 13. Uninterrupted progress. Soon after he left the hospital well.



CASE II



CASE III

CASE III (Vol. xlvii, Case 6917).—Female, aged twenty-eight years. Admitted September 19, 1909. Duration of illness, about one month. Fairly severe attack.

September 26. Very drowsy and slept most of the day. Tongue drying. Some diarrhea (5). Abdomen distended.

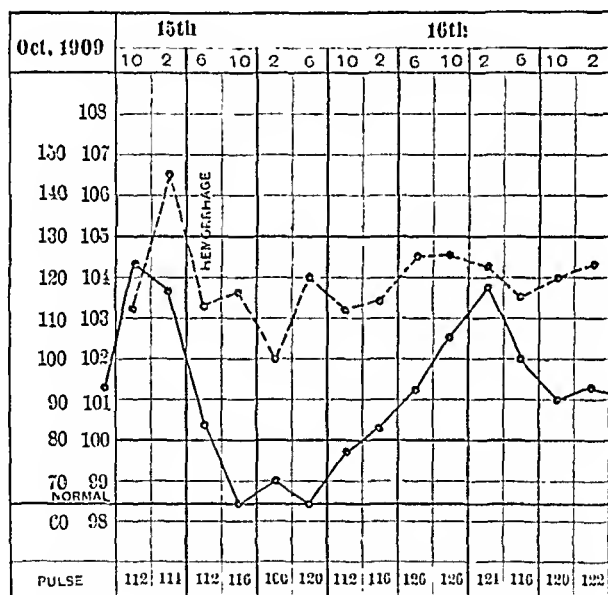
September 29. Abdomen distention marked. Pulse dicrotic. Patient very dull.

October 1. Hemorrhage occurred in night and today several times. Pallid. Skin cold and clammy. Pulse of poor quality. Respiration sighing.

October 2. No more hemorrhage. Patient brighter.

October 4. Abdomen distended. Respiration sighing. Pallor marked but pulse unchanged. Resting well at night.

October 5. Slight hemorrhage today. This patient eventually left the hospital well.



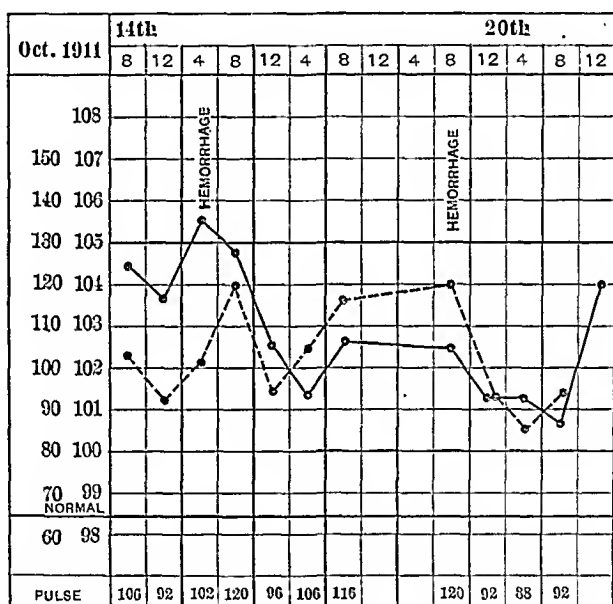
CASE IV

CASE IV (Vol. xlvii, Case 6926).—Male, aged thirty years. Admitted September 30, 1909. Duration, five days. Severe case, with high fever, easily lowered always by three grains of aspirin.

October 14. Has a restless night; tried to get out of bed, and talked to himself. Subsultus marked. Sweated freely. Very drowsy, but rational until tonight; sitting up in bed and trying to get out of it. 8 P.M.: pulse 120; respiration, 20; temperature, 105°, 10 P.M.: pulse, 104; respiration, 20; temperature, 100.2°. Pulse and abdomen good.

October 15. Profuse hemorrhage at 6 A.M., which was bright red. Pulse irregular and intermittent, small and thready. Profuse sweating. 8 A.M.: pulse, 144; respiration, 32; temperature, 103.2°. At noon patient was quite bright; pulse, 112; respiration, 24; temperature, 100.2°. 4 P.M.: pulse 116; respiration, 28; temperature, 98.2°. 8 P.M.: pulse, 120; respiration, 20; temperature, 99°. Pulse of better quality. Another hemorrhage in evening. Midnight: pulse, 120; respiration, 20; temperature, 98.3°.

October 16. Noon: pulse, 120; respiration, 24; temperature, 101.1°. Patient brighter. Pulse of better quality than in morning. Patient very quiet; slept most of the day. Abdomen and pulse satisfactory. After this the patient had a number of hemorrhages at intervals of several days. Each one was followed by a temporary drop in temperature and pulse-rate and an improvement in general condition. He eventually completely recovered.



CASE V

CASE V (Vol. lxxiv, Case 9772).—Male, aged twenty-six years. Admitted October 9, 1911. Duration of illness, ten days. Dull and heavy, and covered with rose spots. Lips dry. Temperature, 104.8°.

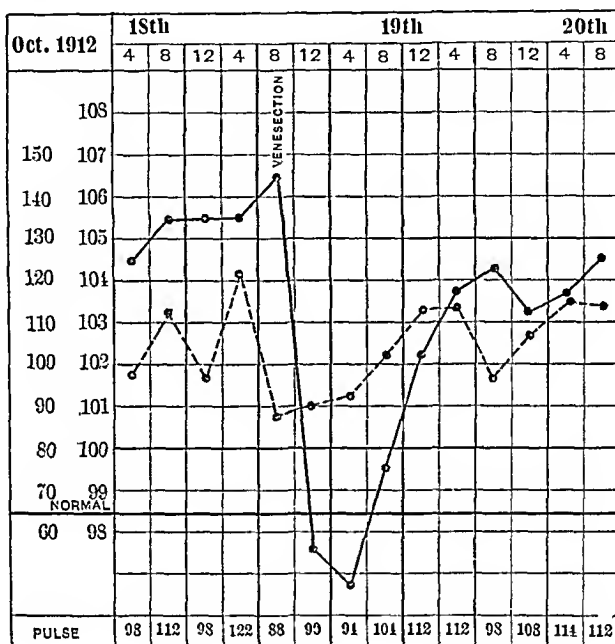
October 14. Very dull and heavy. Perspiring freely. Respiration, 36; pulse, 105. Had a free hemorrhage this morning.

October 15. Patient appears to be improved; less toxic. Tongue very dry.

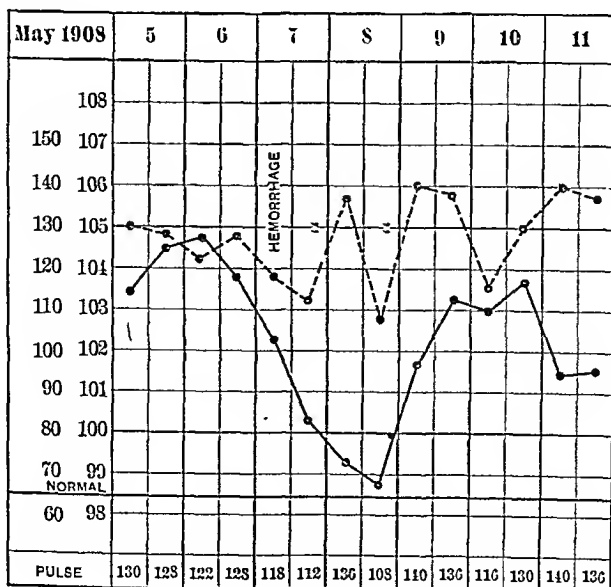
October 16. Pale and hard to arouse. Had two hemorrhages. Twitching of eyebrows and mouth. Tongue very dry.

October 19. 9 A.M.: temperature, 99°; pulse, 88. Listless and weak. Muttered at times. Tongue dry and reddish brown. Lips dry. After this she continued very ill, but less desperately so, and by the end of the month was much better and left the hospital well before the end of the year.

CASE VIII (Vol. xxv, Case 4210).—Female, aged thirty-two years. Admitted April 28, 1908. Duration, ten days. Was very ill on admission.



CASE VII



CASE VIII

May 1. Temperature high. Delirious and weak.

May 7. Hemorrhages early in morning and again at 1 P.M. Blood dark and not in large quantity. Abdomen much distended.

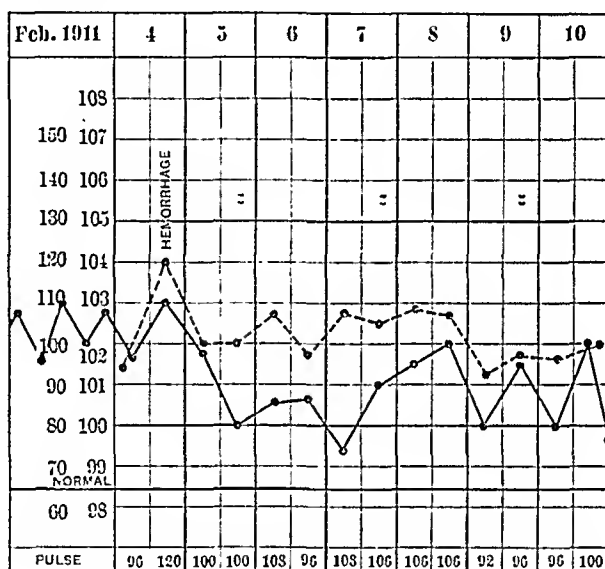
May 8. Another hemorrhage (slight) at 11.30. Distention still marked. A free hemorrhage at 6.15 P.M. Pulse much as before.

May 10. Pulse weak. Restless and unconscious most of time.

May 13. Marked improvement in last two days.

May 19. Weaker, and died at 5.15 A.M.

CASE IX (Vol. lxiii, Case 8870).—Male, aged thirty-one years. Admitted January 19, 1911. Duration of illness, about nine days. Fairly well on admission. Was evidently near the end of the attack. Temperature, 100°, and was soon normal. A week later



CASE IX

had a relapse, and on February 4 a hemorrhage. On day before was dull and sleepy. Systolic blood pressure, 110. Slight bloating. Lips crusted and tongue red and beefy. Had another hemorrhage on February 5 and again on February 7 and 9. After that the patient steadily improved and left the hospital well on March 25.

CASE X (Vol. xxxi, Case 5145).—Male, aged twenty-two years. Admitted October 22, 1908. Had been ill for two weeks. Weak; sleepy; delirious; hard to arouse.

October 28. Had a hemorrhage.

October 30. Had a hemorrhage.

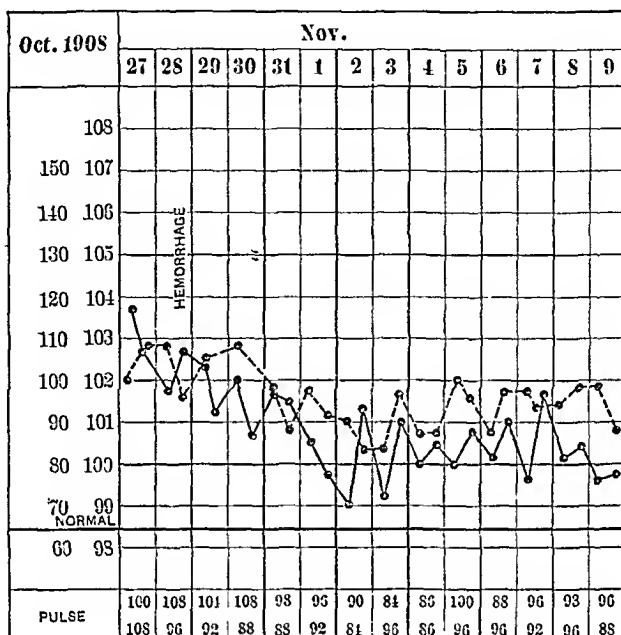
November 1. Not so delirious; taking nourishment well.

November 4. Able to speak. Recovered without further complications.

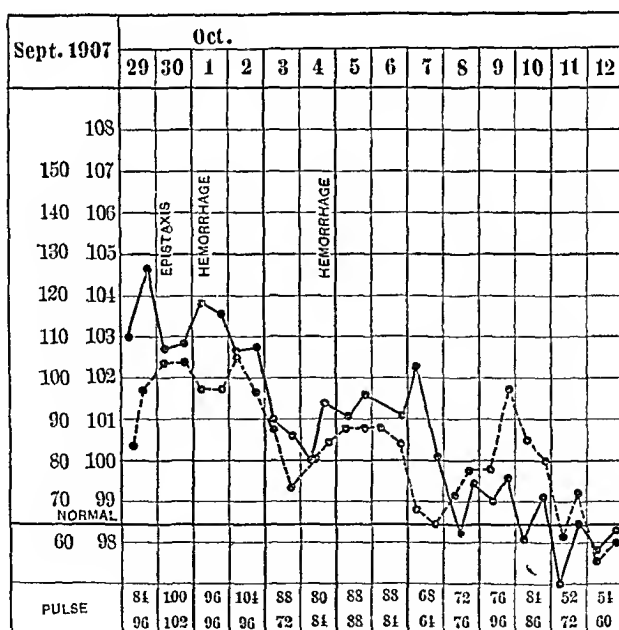
CASE XI (Vol. xviii, Case 3302).—Male, aged twenty-two years. Admitted September 23, 1907. Had been ill for three weeks when admitted; feeling better. Pulse showed marked dirotism.

September 30. Epistaxis; feeling better.

October 1. Slight hemorrhage from bowel. Pulse and temperature not affected by it.



CASE X



CASE XI

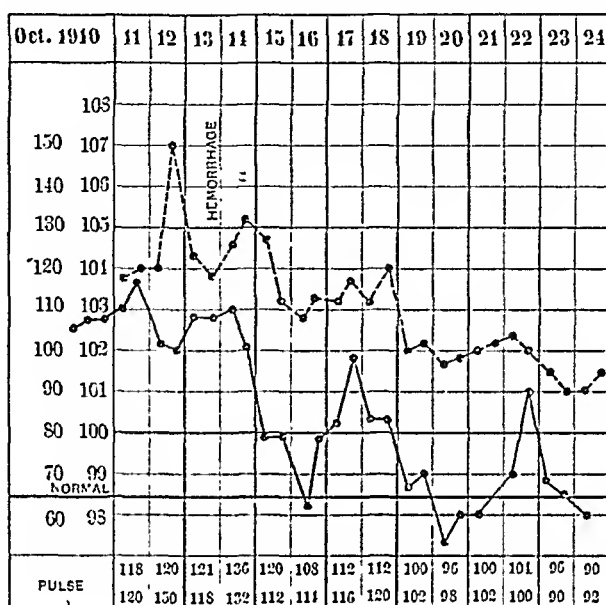
October 4. Another slight hemorrhage.

October 5. Systolic blood pressure, 120.

October 10. Another epistaxis. Feeling well.

November 2. Discharged well.

CASE XII (Vol. lxiii, Case 8691).—Male, aged twenty-four years. Admitted September 19, 1910. Had been ill for four weeks. Very ill and drowsy; pallid; tongue dry and coated.



CASE XII

October 11. Nervous and trembling; very toxic; involuntary evacuations. Looked almost moribund. Drowsy and stupid. Lungs showed a consolidation at the right base. Extremely ill.

October 13. Very ill; profuse hemorrhage today.

October 14. More clots in stools.

October 15. Much better. Lung condition clearing. Pulse, 106 to 122; temperature, 98.2° to 99.2°. Had a good day, but did not rest so well during the night.

November 3. Doing well. Temperature and pulse normal. Was discharged well on November 27.

RECONSIDERATION OF THE QUESTION OF EXPERIMENTAL HYPERTROPHY OF THE THYROID GLAND, AND THE EFFECT OF EXCISION OF THIS ORGAN UPON OTHER OF THE DUCTLESS GLANDS.¹

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THE space allotted is so short that I cannot do more than indicate in merest outline a few of the problems which have presented

¹ Read, by invitation, May 7, 1913, before the Association of American Physicians at the Ninth Triennial Session of the Congress of American Physicians and Surgeons.

themselves in the course of our study in animals and the human subject of the functions of some of the glands of internal secretion.

Twenty-five years ago, in the course of experiments upon the dog, undertaken chiefly with a view of determining the cause of death after operations upon the thyroid gland, I was surprised to find that excisions or transplantations or simple manipulations of the thyroid lobe were, after a time and almost invariably, followed by increase in the size of the remaining portions of the gland, wherever situated.

Examination of the hypertrophied tissue revealed the most unexpected and astonishing histological picture, a structure so different from the normal gland that not one of the several eminent pathologists in this country and abroad, to whom I showed the sections, was able to identify it. The histological changes which resemble those found in exophthalmic goitre are now so well known as not to require mention at this time. With few exceptions this hypertrophic picture made its appearance within twenty-two days after operation of any kind upon the thyroid gland, and even in its most advanced type was observed so late as ninety-five days after operation.

My observations have been confirmed by many, most carefully and convincingly by Marine, and the hypertrophy has generally been regarded as compensatory.

In my original article I expressed the view that possibly some form of auto-intoxication might account for the hypertrophic changes, and for some years have thought that the hyperplasia of the remaining thyroid tissue which has followed excision of a portion of the gland might possibly be due to infection of the wound, and for the following reasons:

1. The increase in the size of the remaining thyroids and the degree of hyperplasia as indicated by the histological picture seemed to bear no relation to the amount removed. The excision of so little as one-fourth of one lobe might be followed by great increase in the size of both lobes, and by the histological changes which characterize hyperplasia.

2. In 1888 I found that hypertrophy of the thyroid glands of dogs occurred after the injection of several cubic centimeters of a bouillon culture of *Staphylococcus aureus* into the peritoneal cavity, and also when a mild form of peritonitis had been produced in these animals—a peritonitis which was not rapidly fatal.

3. Experiments conducted in 1906 and 1907, in the Hunterian Laboratory, seemed to indicate that for the successful transplantation of a parathyroid glandule a considerable deficiency must be created.

4. Twice in the course of the past five years I have had opportunity to examine the remaining lobe of the thyroid gland after

excision of the other in dogs whose wounds had healed throughout without suppuration, and have noted that there was no hyperplasia of the former.

5. From a restudy of the report of my experiments on extirpation of the thyroid gland made in 1888, I find that for the major part of the experiments the wounds of the dogs were left open, and that after twenty-two days, with few exceptions, there was hypertrophy, macroscopic and microscopic, of the remaining gland in the animals whose wounds were permitted to heal by granulation, whereas when the wound healed *per primam* the hyperplasia of the remaining thyroid tissue developed perhaps less regularly and not to the same extent.

6. Manifestations of hyperthyroidism may develop promptly after tonsillitis, appendicitis, pneumonia, typhoid fever, and other infections.

In October, 1912, I proposed to Dr. Hunnicutt that he undertake a series of experiments with a view of determining the matter definitely. Observing aseptic precautions in the strictest manner, Dr. Hunnicutt has made a large number of experiments on dogs, and we are able to report that in none of the thyroids thus far examined has there been the slightest evidence of hyperplasia. The average time allowed to elapse between the removal of the first and second lobes was fifty-five days, the shortest interval being thirty and the longest eighty-one days.

That, nevertheless, there is such a thing as true compensatory hyperplasia of the thyroid gland is proved, I think, by my experiments in transplantation of the parathyroid glandules; which were conducted with the strictest aseptic precautions. Thus when both thyroid lobes and the four parathyroid glandules have been removed and only a film of thyroid transplanted with one parathyroid body, this film hypertrophies enormously, and on microscopic examination displays the typical changes of extreme hyperplasia. In one instance in which the graft was examined fifteen months after operation, the transplanted film had become as large as a good-sized pea.

If it should become a definitely established fact that true compensatory hyperplasia of the thyroid occurs only after the removal of a considerable part of this gland, and that infection or diet or some unknown factor has been responsible for most of the hypertrophies hitherto recorded, investigations are then made possible which could not be undertaken to any purpose if hyperplasia might be expected to follow operative interference of almost any sort upon the thyroid lobe.²

Although expecting that in wounds which healed by first intention

² In 5 unvaccinated dogs operated upon without precautions and whose wounds were left open, there was, greatly to my surprise, not the slightest indication of hypertrophy of the remaining lobe after thirty days.

hyperplasia might not develop after excision of small portions of one thyroid lobe, it surprised me to find from this year's experiments that so much as one and a half lobes may be removed without appreciable effect upon the remainder of the gland, and for the moment my interest in the search for an explanation of the entire absence of any sign of hypertrophy in the experiments of the past winter is as keen as it was years ago to explain the invariable hypertrophy which followed almost any sort of operative interference with the glandula thyroidea. Dr. Marine, replying a few days ago from Vienna to a letter in which I asked for his opinion, writes: "I am anxious to know whether you used iodine in the sterilization of the skin. This, as you know, inhibits to a marked degree compensatory hyperplasia following partial removal just as it does any physiological outgrowth. After trying all sorts of ways to check your 1888-1889 results we always got exactly what you then reported, and I shall have to have very conclusive evidence before being convinced that your results obtained in 1888 could be explained on the bases of wound infection." . . . "You have doubtless controlled the diet as a factor in compensatory hyperplasia."

In most of our experiments the skin has been disinfected with iodine, but in numerous instances it was not.

In 1888 our dogs were fed chiefly on raw meat, whereas during the past year their food has consisted almost exclusively of corn bread and cooked lungs of beeves. From the observations of David Marine, Reid Hunt, Chalmers Watson and others, which bear on this subject, it seems not unlikely that in the diet may be found the solution of the problem.

Should we find that, as a rule, three-fourths or more of the entire gland must be removed before the hyperplastic changes develop, this will be additional evidence to strengthen the belief that the thyroid gland is normally in a state of relative inactivity, and that it is an organ with great reserve power, capable of responding promptly, almost instantly, to certain stimuli.

Of particular interest in this connection are the experiments, just published, of Dr. Reich and Prof. Blauel, of Vienna. They find that in rats, whose thyroids normally have cuboidal epithelium, compression of the trachea is followed by flattening of this epithelium, to an extreme degree. If the oxygen-deprivation induced by the obturation of the trachea should prove to be the cause of the regressive or hypotrophic changes, might we expect to find that the colloid goitres which produce a great degree of tracheal stenosis are less likely to become Basedowified than those which are not accompanied by symptoms of suffocation?

Among the queries which present themselves at the moment are the following:

1. Must a deficiency be created for the successful grafting of ductless glands? Biedl claims to have successfully transplanted two parathyroid homografts in a dog which had not been deprived of any of its parathyroids. To justify his position, he states that all depends upon how long a transplant must live in order to be called a successful one. It seems to be an unchallenged proposition that a transplant cannot live unless it is functioning. But what is meant by functioning? Are tissues growing *in vitro* performing a function? Are the spirals of elastic tissue which we wind about the aorta functioning for a time? For about two months these spiral bands seem to live and continue to constrict the artery, but in six months they are almost absorbed.

2. What proportion of both thyroid lobes is it necessary to remove in order to produce hyperplasia of the remainder? The removal of one and one-half lobes has not been followed by hypertrophy in our experiments of this year.

3. Can a graft live without showing the hyperplastic picture? In other words; will a graft be absorbed unless the deficiency created is so great that hyperplasia must develop? Should the fact that a surviving graft retains the normal structure be taken as evidence that it will be absorbed (that its life will be short of duration)? And could a graft with such dubious existence be stimulated to hypertrophy and to prolonged life by the introduction of conditions which might demand of the thyroid increased function?

If we are still in doubt as to the cause of the hypertrophy of the thyroid glands in our experiments of twenty-five years ago, and are unable to explain its entire absence in our dogs of this past winter, after making scores of experiments to determine the effect of the removal of part of one gland on the remainder of the same organ, how infinitely greater are the difficulties incident to the explanation of the effects upon ductless glands other than the one surgically attacked.

Hypertrophy or enlargement of the hypophysis, for example, described by many authors as following thyroidectomy, has been observed in various parts of the gland: in the anterior lobe, in the pars intermedia, and even in the pars nervosa. There are conflicting views as to the changes which take place both as to situation and histological detail. By most investigators the formation of colloid is emphasized, and this has been interpreted by several as signifying a taking on by the hypophysis of the function of the thyroid; the colloid in the former replacing this substance lost in consequence of the thyroidectomy.

But when experimental hyperplasia of the thyroid takes place, the colloid, instead of being increased in the remaining hypertrophied lobe, is diminished or disappears altogether; and this being the case, it would seem strange that, after thyroidectomy,

it should appear in compensating fashion in the pituitary gland. We think of the normal thyroid, with its large follicles filled with colloid, relatively dense and deeply staining, as being in a state of comparative inactivity or rest; and the histological changes which have been stimulated in one gland by the removal of another have usually been considered as representing hyperactivity of this gland. But to me it appears unlikely that the colloid in the hypophysis which it is assumed makes its appearance in response to thyroid deficiency should signify hyperactivity of that organ, when the same colloid in the thyroid is found in abundance only in the comparatively inactive period of this gland.

It seems to be a natural inference that the loss of one gland of internal secretion should lead to the compensatory hypertrophy of another; and should colloid make its appearance in the eagerly observed unaccustomed places after the removal of a gland which normally is composed chiefly of colloid, the evidence for the compensatory nature of the change would seem to be so complete as to make further substantiation unnecessary. But I am quite sure that the evidence for the current view is not conclusive.

Is it not more probable that the elimination of the function of the thyroid may lessen, directly or indirectly, the demands on other of the ductless glands, and that the colloid changes noted in the hypophysis and parathyroids after thyroidectomy may signify hypo- and not hyperactivity of these organs?

A contribution by Kummer,³ of Geneva, to the study of post-operative tetany, presented at the Twenty-fifth Session of the Congrès Française de Chirurgie, Paris, 1912, is worthy of unusual consideration. A woman, completely deprived of the cervical thyroids and parathyroids, was kept alive for two years.

The autopsy was made by Prof. Askanzy,⁴ who found in the hypophysis changes which seem to be identical with those described by William G. MacCallum⁵ as having been present in the hypophysis of one of my dogs fifteen months after the removal of both

³ Contribution à l'étude de la Tétanie postopératoire. Extrait des Comptes Rendus du 25^e Congrès de l'association Française de Chir., 1912.

⁴ Quotation from Askanzy: "*Hypophyse*. Les cellules chromophiles ou éosinophiles sont très abondamment développées, d'une richesse même extraordinaire. Par contre il n'y a pas d'augmentation de substance colloïde dans les amas cellulaires de l'hypophyse, comme cela se voit dans les hypophyses chez les myxoédémateux. C'est seulement près de la partie nerveuse d'ailleurs intacte, dans la zone intermédiaire soit médullaire, que l'on constate quelques follicules à substance colloïde conformément à l'aspect ordinaire."

⁵ Quotation from MacCallum: "The hypophysis shows rather distinct alterations. The pars nervosa is practically surrounded in the section by the pars intermedia which is perhaps slightly thickened and contains one or two alveoli full of colloid. The pars anterior is in part very deeply stained with eosin, but one portion, and that the major part, is sharply marked off from this eosin-stained tissue by its lilac color. It contains only a few of the bright staining cells, but for the most part is made up of swollen, faintly granular, pale stained cells. These resemble very closely the section obtained by Dr. Homans after injecting pilocarpin. The cleft in the glandular part of the hypophysis is here seen to open into the subarachnoid space." Halsted, Jour. of Exp. Med., 1912, xv, No. 3, 209.

thyroid lobes and of the four parathyroids. This dog, kept alive for this long period by a parathyroid autograft only 14 mm. in diameter, died of tetany on the removal of the transplant.

Rarely again should there be an opportunity to study on the human subject the effects, after two years, of the complete removal of the thyroid and parathyroid glands.

We have never observed hypertrophy of the transplanted parathyroids even when total thyroidectomy and total parathyroidectomy have been done. I am not prepared, at present, to report the results of operations to determine the effect, if any, upon the thyroid of excision of the parathyroids; but I am not quite willing to accept as proved the observations of others who claim that after thyroid lobectomy the parathyroids are stimulated to compensatory hypertrophy, forming follicles containing colloid. *Why should the excision of an amount of thyroid insufficient to bring about thyroid hyperplasia cause compensatory hyperplasia of the parathyroid glandules? And, granted that changes may have occurred in the glandules after thyroid lobectomy, should these consist in the formation of a colloid equivalent to the colloid of the thyroid alveolus if the thyroid-colloid disappears in cases of definite privation and if the accumulation of colloid seems to signify a state of normal or hypo- rather than of hyperactivity?*

Furthermore, if hypertrophy of the parathyroids really occurs after thyroidectomy, might it not be due to the unintentional destruction of some of the parathyroids, or even to infection of the wound? I have never observed hypertrophy of a transplanted parathyroid gland. The tendency of these grafts, in my experience, is always to atrophy.

An enormous amount of experimentation must be done before these questions, which are in no sense remote, can be answered. There are hundreds of eager workers in this fascinating field at present who may add immensely to the confusion, before, from the chaos, order eventually can emerge and the simple laws be established of which perhaps we are not even beginning to dream.

Hypertrophy of the thymus gland has frequently been observed in Graves' disease, and from our observations during the past ten or eleven years of a considerable number of such cases in which the greater part of both thyroid lobes has been removed, we think there is reason to believe that the thymus atrophies in consequence of the operation upon the thyroid. The lymphocytosis gradually disappears, and in none of the earlier cases which have presented themselves this past year for examination has the thymus been skiagraphically visible. It would seem, therefore, that the thymus may be activated by the thyroid.⁶

⁶ Support to this view is given by the results of the experiments of A. L. Tatum reported since the reading of this paper (*vid.* Jour. Exp. Med., June 1, 1913). Tatum finds that in rabbits the thymus atrophies after excision of the thyroid gland.

AURICULAR FIBRILLATION: CLINICAL OBSERVATIONS ON PULSE DEFICIT, DIGITALIS, AND BLOOD PRESSURE.

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RECENT studies with the electrocardiograph on animals under experimental conditions and on the human subject have permitted the separation of a group of cardiac irregularities known as "auricular fibrillation," which is of great clinical importance. So clear is the clinical picture of this group that in nearly every instance the graphic records are unnecessary, and the ear and the finger are quite adequate to make a correct diagnosis. The clinical importance of this group is two-fold: (1) In it are included fully one-half of the serious cardiac irregularities which one sees, and (2) these are the cases which are almost invariably benefited by the administration of digitalis. A careful clinical study of a large number of cases of auricular fibrillation in hospital and private practice has prompted us to present the following points, which our experience has demonstrated to be of practical value in treating these patients intelligently and successfully.

The palpation of the radial pulse is a very insufficient criterion of the condition of the circulation. While the palpation of the pulse alone may be sufficient to establish a diagnosis, and while by this method one immediately detects the complete irregularity in force and frequency which characterize this group, the count of the radial pulse may be misleading. Frequently the number of the impulses which can be counted at the wrist is far below the actual number of cardiac contractions. Only those waves which are of considerable volume and force can be felt at the wrist, and many small ventricular contractions expend their force before reaching the radial, and some even fail to open the aortic valves. These small contractions are ineffectual in maintaining an adequate circulation, yet are exhausting to the heart muscle, for we know that, in accordance with the law discovered by Bowditch, every contraction of heart muscle is maximal: that is to say, if it contracts at all, it exhausts all of the energy stored as contractile material in its muscle fibers at any particular moment; hence it is evident that however small a contraction may be, it must be taken into

consideration in estimating the gravity of the condition of any particular heart.

The inadequacy of the observations on the radial pulse alone is well illustrated in Fig. 1. Here the lower margin of the shaded area indicates the radial count; if one were guided by this alone, one would have said that on admission the cardiac rate was under 70 and never above 100. The upper boundary of the shaded area is the count taken by auscultation at the apex, and represents much more accurately the true condition, the admission rate being 127; the gradual reduction to the neighborhood of 60 makes the real improvement apparent.

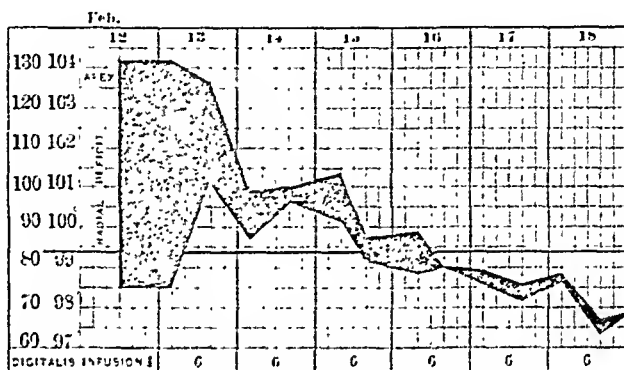


FIG. 1.—The shaded area represents the pulse deficit; the upper edge is the apex rate; the lower edge is the radial rate. Figures in digitalis column indicate dosage of the infusion in drams per twenty-four hours. Patient in bed during period represented in the figure.

The term "pulsus deficiens" has for a long time been used in describing pulse phenomena (Traube, Hering, Wenckebach, etc.), but each author has used it with a different meaning: some have considered it synonymous with "pulsus intermittens," others have applied it to an absence of ventricular contraction, which breaks the ordinary rhythm; it has been used in describing extrasystoles and pulse alternans.

So far as we know, Drs. Robinson and Draper, of the Rockefeller Institute, first used the term "pulse deficit" to designate the difference in the count when taken at the apex and in the carotid artery. *By "pulse deficit" we mean the difference between the number of cardiac contractions and the number of impulses which can be palpated in the radial artery.* The best way of determining the pulse deficit is to have the apex counted by auscultation by one observer while another is simultaneously counting the radial (these observations must cover a period of not less than a full minute, on account of the extreme irregularity of the pulse in many of these cases a count of one-quarter or one-half minute only is much less accurate). When one is obliged to make these observations unaided, the apex and the radial counts may be made

in successive minutes. This of course does not give an absolutely accurate deficit, but it is extraordinary how closely the counts of successive minutes will coincide even when the heart and radial show the most extreme degrees of irregularity. After a little practice one may be able simultaneously to auscultate the apex and palpate the radial, thus determining the number of beats which fail to reach the wrist in the period of a minute.

In the figures the upper margin of the shaded area represents the apex count, the lower margin the radial count, and the width of the shaded area represents the deficit at any particular point in the curve.

It is now generally recognized that the cases of auricular fibrillation are those which best respond to the administration of digitalis and drugs of this group. The mechanism by which digitalis acts in these cases is not entirely understood, but it is believed to have a direct influence in increasing the contractile power and tone of the ventricular musculature; besides this, it so affects the tissues junctional between the auricles and the ventricles that a portion of the irregular shower of impulses from the auricle are blocked, thus reducing the frequency of ventricular stimulation, allowing the ventricle to recover more completely, and to contract less frequently and with greater power. During each diastolic period thus lengthened the heart is better filled with blood which is more completely expelled during each systole.

The result of giving digitalis in these cases depends not so much on the form in which it is administered (tincture, extract, infusion, etc.) as on the amount and concentration of the active principles which each preparation contains. The effective method of its administration is to give enough of any particular preparation to obtain the physiological effect; the size of the dose necessary for any individual patient cannot be told in advance, but must be determined by its physiological effect in each case.

It is here, we believe, that a study of the "pulse deficit" is of great clinical value. A reduction in the degree of the deficit is the best indication of the effectiveness of the particular dose in the individual case.

When the deficit is abolished the digitalis must be discontinued or the dosage greatly diminished. Mackenzie, in his monograph on *Digitalis*¹ advocates the use of digitalis in auricular fibrillation until the physiological effects are evident. His method is to push the drug until the patient complains of nausea or until the characteristic coupled beats of the cardiac rhythm appear. Since we have been following our patients, guided by observations on the pulse deficit, we have usually been able to avoid the production of both nausea and the coupled beat, and while these symptoms occur

¹ Heart, 1911, vol. ii, p. 278.

sionally appear, they are exceedingly rare. We are accustomed to continue the administration of digitalis as long as there is any considerable pulse deficit, and the dosage for the individual is so regulated that the pulse-rate is kept without deficit, and as near to 70 as possible. We have often given digitalis continuously in this way for a period of two years or over (see Fig. 3).

Another advantage of "pulse deficit" observations is the information it gives of the activity of any particular digitalis preparation; we have found it a simple method of making a physiological assay of particular preparations. If after a short period the "pulse deficit" is not diminished, we are apt to conclude that the preparation is inactive. As a rule, we have obtained the best results with an infusion, freshly made each day from the best English leaves.

The relative deficit. In many cases of auricular fibrillation, particularly where improvement has occurred and the heart has become less irregular, slow, and fairly compensated, it will be found that the count at the apex and the radial are identical. Even in these cases the individual waves show a considerable variation in force and size. This is brought more clearly to view if the cuff of a blood-pressure apparatus is placed on the arm and the radial is counted while varying degrees of pressure are applied through the cuff. This difference in the pressure values of successive waves we have termed the "relative deficit," as contrasted with the absolute deficit, when without brachial pressure some waves fail to reach the radial.

The following observation will serve to illustrate this point: The patient was a gentleman who had fibrillating auricles for something over two years, with at times an apex rate of 180 and an absolute deficit of over 50. His heart was fairly compensated, and he was able to supervise large business interests which required a daily attendance at his office of six to eight hours. When we last saw him his apex rate was 64, radial rate 64, deficit 0. On applying the brachial cuff the following counts were obtained:

Brachial pressure.	Radial count per minute.
140 mm.	0
130 mm.	50
120 mm.	58
110 mm.	62
100 mm.	64

While he had no absolute deficit, his relative deficit was quite evident when the pressure values of the waves of one minute were thus studied. This relative deficit may be detected in all cases of auricular fibrillation; it is rarely seen in other cardiac arrhythmias. We have found that such observations on the relative deficit are of real diagnostic value in corroborating a condition of auricular fibrillation which palpation and auscultation have led us to suspect.

The usual way of estimating *blood-pressure* is entirely fallacious in auricular fibrillation. The accustomed method of obliterating the brachial artery by cuff-pressure and then by gradually lowering the pressure to determine the systolic blood-pressure by the height of the mercury column at which the pulse wave below the cuff is detected by palpation or auscultation is obviously of little value when practically each pulse wave has a different pressure value. Mackenzie, in his recent monograph on *Digitalis*,² says "we gave up the attempt to register the blood-pressure in cases of auricular fibrillation, for though some sort of result could be obtained, the result would be expressed by a figure, and this would have given an aspect of precision, which it did not possess, and would therefore inevitably mislead."

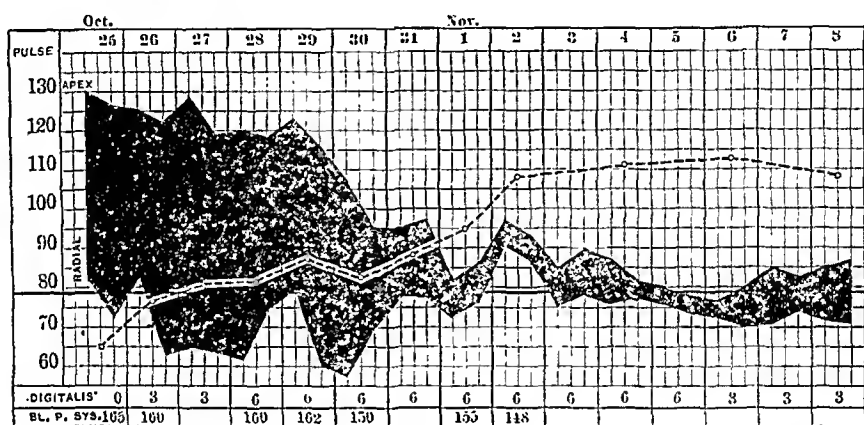


FIG. 2.—The shaded area represents the pulse deficit; the upper edge is the apex rate; the lower edge the radial rate; The broken line indicates the "average systolic blood-pressure" (compare these values with the figures at the bottom of the chart which show the systolic blood pressure determined by the usual method). Figures in the digitalis column indicate drams of the infusion per twenty-four hours.

If such a pulse is observed for a period of a minute it will be found that only a small fraction of the total number of cardiac contractions have a pressure value, approximately the systolic blood-pressure as determined by this method. Fig. 2 illustrates the inaccuracy of this method in these cases. Systolic blood-pressure taken by the usual method would signify that the successive blood-pressure of this patient were 165, 160, 160, 162, 150, 155, 148, etc., and that as her condition improved the blood-pressure was lowered. As a matter of fact, only a few beats could be detected below the cuff when exerting a pressure at these levels, and while doubtless her systolic blood-pressure was momentarily at these levels, they in no way indicate the efficient pressure of the blood column. As we shall show later, her systolic blood-pressure really increased with the improvement in her condition.

² Heart, 1911, vol. ii, p. 283.

A much more valuable estimate of the force of the blood-stream can be obtained by estimating the blood-pressure by another method; the average systolic blood-pressure.

To obtain what for convenience we have termed "*the average systolic blood-pressure*," the apex and radial are counted for one minute, then a blood-pressure cuff is applied to the arm, and the pressure raised until the radial pulse is completely obliterated; the pressure is then lowered 10 mm., and held at this point for one minute, while the radial pulse is counted; the pressure is again lowered 10 mm., and a second radial count is made; this count is repeated at intervals of 10 mm. lowered pressure until the cuff-pressure is insufficient to cut off any of the radial waves (between each estimation the pressure on the arm should be lowered to 0). From the figures thus obtained the average systolic blood-pressure is calculated by multiplying the number of radial beats by the pressures under which they came through, adding together these products and dividing their sum by the number of apex-beats per minute, the resulting figure is what we have called the "average systolic blood-pressure." The following two observations made on a patient will indicate the method of computation:

B. S., April 29, 1910. Apex, 131; radial, 101; deficit, 30.

Brachial pressure.	Radial count.
100 mm.	0
90 mm	13 $13 \times 90 = 1170$
80 mm	$47 - 13 = 34 \times 80 = 2720$
70 mm	$75 - 47 = 28 \times 70 = 1960$
60 mm	$82 - 75 = 7 \times 60 = 420$
50 mm	$101 - 82 = 19 \times 50 = 950$
	Apex = 131)7220
	Average systolic blood-pressure 55+

B. S., May 11, 1910. Apex, 79; radial, 72; deficit, 7.

Brachial pressure.	Radial count.
120 mm.	0
110 mm.	44 $44 \times 110 = 4840$
100 mm.	$64 - 44 = 20 \times 100 = 2000$
90 mm.	$72 - 64 = 8 \times 90 = 720$
	Apex = 79)7560
	Average systolic blood pressure 95+

The estimation of blood-pressure by this method gives us a simple and approximate measure of this factor of the heart's work. The diastolic pressure may be roughly determined by taking a graphic record with the Erlanger or Uskoff instruments and noting the pressure at which the average excursion of the pulse waves is maximal.

The effect of digitalis on blood-pressure in auricular fibrillation.
The effect of digitalis on blood-pressure has long been a matter

of contention. Thirty years ago it was thought that the administration of digitalis elevated blood-pressure, but this view was controverted by many subsequent observers such as Christeller, Fränkel, Heike, Hansen, Gross, Potain, and others. Their opinions have been summarized by Janeway,³ who says: "All of the above observers fail to find any relation between the arterial tension and the circulatory improvement from digitalis."

Our present evidence justifies us in asserting that in the cases of cardiac insufficiency where digitalis is of most value, it raises blood pressure by slowing and increasing the force of ventricular activity.

The failure of former observers to recognize this fact was dependent on two elements: (1) that it was not then known that the benefits of digitalis administration are mainly evident in cases of auricular fibrillation, and (2) that they had no satisfactory method of estimating the blood pressure in these cases in which the successive contractions of the heart vary so greatly in force and time. Mackenzie says in his monograph on *Digitalis*, to which we have referred above, "In our observations, even when the drug was pushed and caused nausea and heart irregularities, we could detect no appreciable effect upon the blood pressure (except in one case)."

Since we have come to recognize that digitalis finds its chief usefulness in cases of auricular fibrillation, and have applied our method of estimating the average systolic blood-pressure to the study of this group, it has become clear to us that hand-in-hand with the improvement in the patient's condition the average systolic blood-pressure is elevated.

This is best made evident by the presentation of several charts, which have been selected from a considerable number, all of which show the same features.

Fig. 2 shows the effect of rest and digitalis on a case under observation in the Presbyterian Hospital for two weeks. The diminution in the deficit and the gradual increase in the average systolic blood-pressure is quite clear. During this period all of the patient's symptoms improved, and she was able to leave the hospital to return to her home.

This chart also shows how misleading would have been the systolic blood-pressure estimations made by the ordinary method (see figures at the bottom of the chart), for at these brachial pressures only four or five waves per minute reached the radial during the three days following her admission. The diagram indicates that the full digitalis effect is not obtained for four or five days; this we have found to be quite usual.

Fig. 3 is the chart of a gentleman who during the whole

³ The Clinical Study of Blood-pressure, New York, 1904, p. 210

period of observation insisted upon following his ordinary occupation; he was not confined to bed at any time, although we should have considered this the wisest course when he was first seen. He therefore illustrates the effect of digitalis independent of the influence of any considerable amount of rest in the horizontal position. All the observations were made by one of us in his office. The rise in blood-pressure coincident with a slowing of the pulse and diminishing deficit and the fall of pressure corresponding to an increase in the pulse-rate and deficit stand out clearly. The observations cover a period of nineteen months, and the changes in the deficit and the blood-pressure could be closely correlated with his other symptoms. Whenever there was any considerable deficit or the blood-pressure fell this was associated with more or less dyspnea, a lack of vigor, and feelings of lassitude.

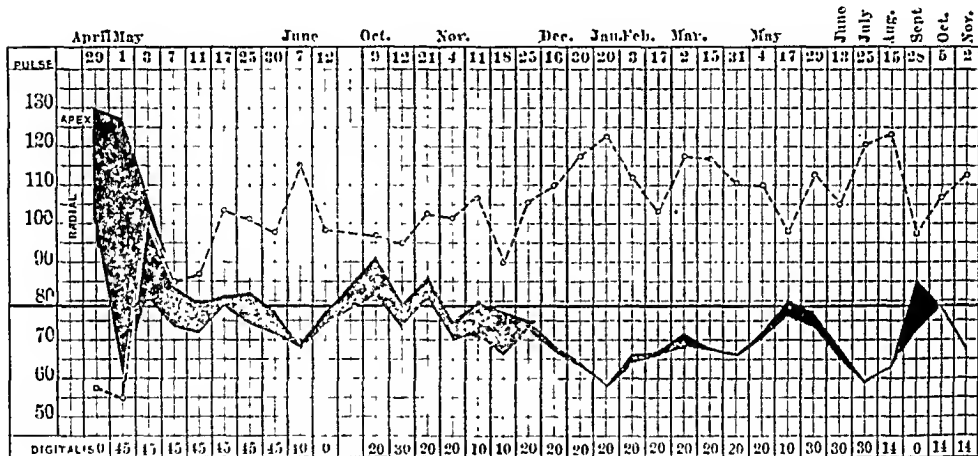


FIG. 3.—The shaded area represents the pulse deficit; the upper edge is the apex rate; the lower edge the radial rate. The broken line is the "average systolic blood pressure." The figures in the digitalis column indicate minims of the tincture per day. Patient not confined to bed.

Fig. 4 is that of a woman who was in the Presbyterian Hospital during the whole period of observation as represented by the diagram. The initial deficit on admission, which showed a marked and sudden diminution with the administration of a freshly made infusion of digitalis (an ounce was given on October 17), the first setback induced by getting out of bed, her subsequent improvement under rest and digitalis, the second setback brought on by an attack of hemorrhoids and the variations in blood-pressure associated with the various stages of her progress, are all indicated in a graphic manner. Unfortunately the blood-pressure observations are not as numerous as one would wish, but the inverse relationship between the average systolic blood-pressure and the pulse-rate and deficit are evident. It is difficult to analyze the last setback, as three elements took part in its production: (1)

the upright position, (2) the withdrawal of digitalis, and (3) the pain attendant on the attack of hemorrhoids and their incision under cocaine. It seems reasonably evident, however, when we compare this with the preceding setback, that the hemorrhoidal discomfort was a considerable factor in aggravating the circulatory deficiency.

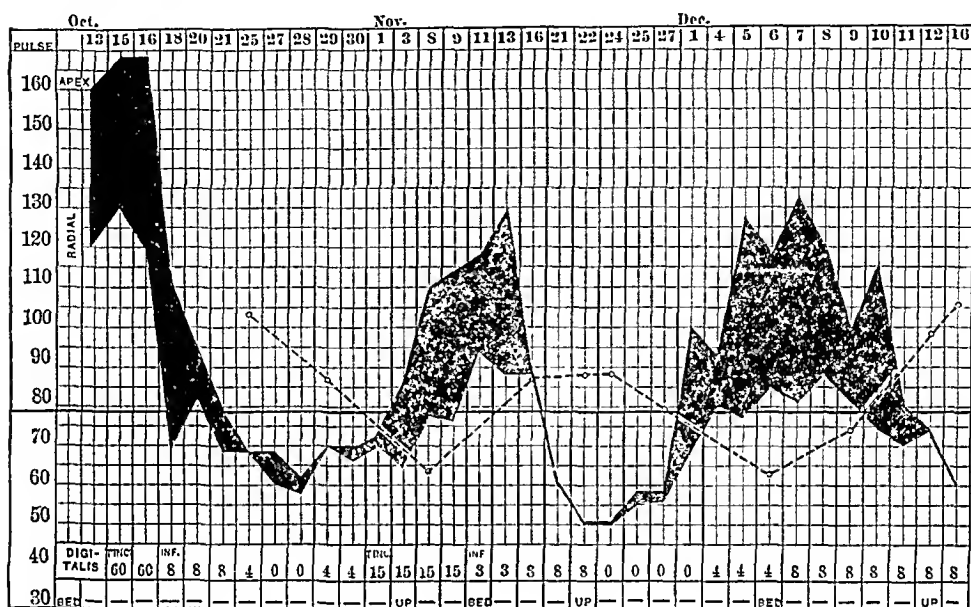


FIG. 4.—The shaded area represents the pulse deficit; the upper edge is the apex rate; the lower edge is the radial rate. The broken line indicates the range of the "average systolic blood pressure." Digitalis figures indicate minims of the tincture and drams of the infusion. October 13, admitted to hospital. November 3, up in chair one-half hour; November 9, up in chair two hours. December 4, up in chair four hours; at this time she had a crop of external hemorrhoids which caused much distress.

CONCLUSIONS. 1. In auricular fibrillation palpation of the radial pulse is a misleading guide to the determination of the condition of the circulation.

2. The pulse deficit is a simple and useful means of following the progress of cases of auricular fibrillation, and of confirming observations on the value of various therapeutic measures, including the activity of various preparations of different drugs.

3. The relative deficit is of value in the diagnosis of suspected cases of fibrillation.

4. The ordinary method of estimating blood-pressure is misleading in cases of auricular fibrillation; it may with advantage be replaced by estimating the average systolic blood-pressure, which gives an approximate measure of the real systolic pressure.

5. The administration of digitalis elevates blood-pressure in cases of auricular fibrillation.

THE MINUTE CHANGES PRODUCED IN LEUKEMIC TISSUES BY EXPOSURE TO RÖNTGEN RAYS.¹

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THE changes produced by Röntgen irradiation in the blood-forming organs of experimental animals have been fully described by Heineke, myself, and other observers. In previous reports² the writer has also described the changes produced in the tissues of leukemic patients by prolonged exposure to these rays. Since that time he has had additional opportunities of examining the tissues of leukemic cases treated in this manner, in all the autopsy material of eight cases of myeloid leukemia, two of lymphoid leukemia, three of Hodgkin's disease, and a number of lymph nodes and spleens taken from such cases. These cases present, therefore, a varied range insofar as the period of irradiation is concerned; in some, the tissues show the early action of the rays; in others, the changes are those produced by irradiation extended over periods of one year, eighteen months, and two years. As a result of this study, it has been possible to separate the immediate and remote effects of the irradiation, and to distinguish the changes so produced into two classes: *immediate* or *degenerative* and *reactive*. A number of interesting observations have been made during the investigation, and it seems worth while to present here in condensed form the total results of these observations.

The immediate action of Röntgen rays upon the tissues of leukemia is a degenerative one. Cells are either killed outright or are so damaged that they die within a short period, both cell body and nucleus showing rather specific changes, so that it is possible to distinguish these degenerative changes from those produced in leukemic tissues by infections or other injurious agents. The cells so injured are the small and large lymphocytes, myelocytes, myeloblasts, large lymphocytes, and to some extent, also, the polynuclears. After a prolonged period of irradiation there comes an apparent period of adjustment to this destruction, the tissues contain fewer evidences of cell death and degeneration, but also fewer proliferating cells. In the blood-stream the number of white cells may decrease to normal or below normal; but it may, on the other hand, steadily rise until the number is much greater than before the irradiation, that is, a leukemic condition of the blood may be reduced to an aleukemic under the progress of the treatment or

¹ Presented before the Section of General Pathology, XVII International Congress of Medicine, London, August, 1913.

² International Clinics, 1906; Trans. Amer. Röntgen Ray Soc., 1906.

the reverse may take place. In the cases dying after prolonged treatment with Röntgen rays the character of the cells in the spleen, lymph nodes, and bone-marrow is different from that of these organs in patients who have received no Röntgen-ray treatment. Upon these differences we base our description as follows:

I. DEGENERATIVE CHANGES. As the result of single exposures, or of several within a relatively short period of time, the tissues of the lymph nodes, spleen, and bone-marrow, in the order given, show patches of degenerating cells, as manifested by nuclear fragmentation and swelling of the cell. In the earliest cases the nuclear membrane of the cells (lymphocyte, myelocyte, etc.) is preserved, the nucleus swollen, with fragmentation of its chromatin, into spherical granules of varying size. The protoplasm may show no changes or become clearer, often vacuolated. The cell so damaged does not show these changes immediately after the irradiation, but usually within ten to fourteen days. The injured cells then rapidly split up into fragments, all traces of the protoplasm are lost, and only the chromatin granules remain, often as "chromatin dust." This injury to the cell is not a diffuse one; apparently only certain cells are affected, as many cells apparently normal are found near the degenerating cells. In the lymph nodes the degenerating cells may be found especially in the germ centres if these are still preserved, but after a time they are found all thorough the node. Repeated exposures cause an increase in the number of the degenerating cells, the greater part of the gland may become necrotic, in some glands all cells may be killed, and a caseous detritus finally takes the place of the cells of the node, the connective-tissue capsule gradually becoming thicker. These changes are more marked in the lymph nodes of Hodgkin's disease and lymphemia than in those of myelemia. In the spleen the reverse is apparently true; the myelemic spleen shows greater cell-degeneration and cell-necrosis than does the lymphemic spleen. The atypical myeloid cells in this condition suffer chiefly, especially the large bone-marrow lymphocytes, or myeloblasts. The myelocytes and cells of the type of bone-marrow giant cells also are easily killed and disappear, until finally all atypical myeloid cells in the spleen may be entirely absent, and the spleen appear as a fibroid organ containing scattered lymphoid cells. The reduction in size of the myelemic spleen may, therefore, be considerable, and in our experience is always greater than that of the lymphemic spleen. Similar degenerative changes occur in the bone-marrow, but are less marked. It is much more apparent in myelemia than in lymphemia.

Lymph nodes removed some months after continued irradiation for short periods daily show in lymphemia and Hodgkin's disease many large cells containing a diffusely staining or granular protoplasm. Areas of cells containing numerous fat droplets begin to appear, and finally the nodes may contain large areas of fatty

degeneration. The vacuolated cells may ultimately go to pieces and large fat droplets remain in the tissue detritus. Cholesterol crystals soon form in these, so that it is not uncommon to find in the irradiated glands of lymphemia and Hodgkin's disease areas of caseation containing fat droplets and cholesterol clefts. Even under the continued irradiation, foreign-body giant cells may develop in these areas. In some glands all of the cells finally assume the type of large, pale lymphocytes, with vacuolated protoplasm. The writer has never found these fatty changes in the lymph nodes of myelomic cases.

In the blood-smears made from myelomic and lymphemic patients the reduction in the number of white cells with a great increase in the number of degenerating forms are the chief changes observable. The reduction in lymphemia is not as striking as it is in myelemia; on the contrary, the number of small lymphocytes in the blood may steadily rise in spite of the irradiation; and in one case of Hodgkin's disease irradiated over a long period of time, the blood which showed no leukemic characteristics at the beginning of the irradiation gradually took on the characteristics of a lymphatic leukemia, with great numbers of large lymphocytes in the circulating blood. There is apparently a limit to the degenerative action upon the white cells and blood-forming organs during irradiation; and after a certain time some adjustment or reaction to the irradiation apparently takes place.

II. REACTIVE CHANGES. The reactive changes are shown by a diminution in the number of degenerating and necrotic cells in the blood-forming organs, and in a change in the type of cells forming the bulk of these tissues. In lymphemia and Hodgkin's disease the reaction takes place much more quickly than in myelemia. Around the necrotic glands in the first-named condition there is regenerated a new and atypical lymphoid tissue characterized by a great number of atypical large lymphocytes, of a character resembling the maternal lymphocytes of hyperplastic germ centres, seen in chronic inflammations of the tonsils and other lymphoid tissues. These cells have a granular cytoplasm, staining more heavily with eosin and hematoxylin, and with granular nuclei. This newly formed atypical lymphoid tissue may infiltrate the capsule of the lymph node and extend into the necrotic area, replacing it in part; or if it begins within the lymph node it may infiltrate through the capsule into the surrounding tissues. New areas of atypical lymphoid tissue develop in the cervical, axillary, and prevertebral adipose tissue. In these new areas vacuolated cells are very common, as are also large, pale cells of endothelial type. Collections of hyperchromatic cells with large irregular nuclei occur throughout this new tissue. In the lymph- and bloodvessels of this tissue there is a great increase in cells of the atypical lymphocyte character.

In the case of myelemia treated over long periods of time the peripheral lymph nodes may show at death little change except a poverty in germ centres and an absence of cells of the bone-marrow group. The retroperitoneal hemolymph nodes may show a marked hyperplasia of atypical cells resembling the large lymphocytes of the bone-marrow. All distinction between the cords and trabeculae and sinuses is lost; the entire gland is made up of densely packed cells that infiltrate through the capsule and into the neighboring fat tissue. The bloodvessels may or may not show any increase in the number of white cells, but usually contain cells of the large lymphocyte type. No other cells of the bone-marrow group are found in these hyperplastic prevertebral glands. I have not found in my cases as marked an atypical regeneration of leukoblastic tissue in the spleen as in these glands. In some cases the spleen is fibroid to the end, with few or no cells that can be regarded as myeloid in type. In two cases large areas of caseous necrosis, hemorrhages, and anemic infarctions, associated with thrombosis of the splenic vessels, were present. One case showing these changes in a marked degree died from a rupture of a splenic artery, the spleen at autopsy being embedded in a large clot proceeding from a small opening in the capsule of the organ communicating with a small-sized artery. The arteries of the spleen showed an obliterating endarteritis, and the majority of the smaller vessels were thrombosed. No myeloid tissue was present in the organ, although the other organs of the body presented the usual appearances of leukemia.

The changes in the bone-marrow resemble those in the retroperitoneal hemolymph nodes in those cases in which the leukemic condition of the blood had changed to an aleukemic under the treatment. Cells of myeloid type were present in greater numbers, but the chief cell of the marrow was the large pale lymphocyte (myeloblast?). In no case treated by Röntgen irradiation were the conditions in the hematopoietic organs changed to a normal condition. The effect of the treatment is essentially degenerative and inhibitive, but the essential leukemic process goes on unchecked, although greatly modified. The treatment is, therefore, not curative; and such a result we no longer expect from our clinical failures.

In the first stages of the treatment the leukemic tissues show great degeneration and destruction of the white-cell-forming tissues. It may completely disappear from the spleen, and the processes of white-cell formation may be so inhibited that an aleukemic condition of the blood may result. After some months there arises a more undifferentiated leukoblastic tissue, particularly in the retroperitoneal hemolymph nodes and in the bone-marrow; the leukemic condition of the blood may return or it may not. With an increasing cachexia the process may be terminated by symptoms of intoxication, or by some secondary event, as hemor-

rhage from the necrotic spleen. The changes in the kidney, which may be very marked (cloudy swelling, simple necrosis, and calcification), may also in part be responsible for the fatal termination.

In conclusion, prolonged irradiation of the hematopoietic organs in leukemia causes first a degeneration of the young and maternal cells, leading to a great decrease in the output of leukocytes, particularly in myelcemia. To this destructive effect there follows a reaction in which cells of a more resistant type are formed, and the essential leukemic process remains unchecked, although altered in character.

CAN IT BE PROVED FROM CLINICAL AND PATHOLOGICAL
RECORDS THAT THE NUMBER OF CURES OF CANCER WILL
BE GREATLY INCREASED BY THE PROPER EXCISION
IN THE EARLIEST PRECANCEROUS OR CANCER-
OUS STAGE OF THE LOCAL DISEASE? ¹

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CLINICAL evidence has gradually accumulated which demonstrates that we can increase the number of cures of malignant tumors.

This evidence has been slow in accumulating, due to many factors. In the first place, patients have sought advice late; both surgeons and physicians in the past have delayed action until the diagnosis of malignancy had become obvious clinically.

In the beginning of surgery of neoplastic lesions the operation, except amputation for sarcoma, was not radical enough, and unfortunately amputation for sarcoma rarely cured the truly malignant tumor, because in these cases metastases take place early, before the local symptoms are sufficiently grave to influence the patient to consent to amputation or to force the surgeon to this mutilating operation.

Resection of the stomach for cancer by Billroth was perhaps the beginning of radical operations for malignant disease followed later by the complete operation for cancer of the breast (Halsted's method, 1889). The better results of the latter operation as compared with simple removal of the breast for cancer were soon known.

As surgeons have operated more radically and as patients have sought advice earlier the number of cures of cancer and sarcoma has increased.

In the past a radical operation was spectacular, bloody, involved

¹ Read before the American Association for Cancer Research, Washington, D. C., May, 1913.

great risk to life, and often mutilated. But when these operations were performed for malignant disease in the later stages they were not really radical, because the disease was rarely, if ever, completely removed.

Today the word "complete" is a better term for the proper operation for malignant tumors.

In the surgical pathological laboratory of the Johns Hopkins Hospital we have kept complete records of all cases from which pathological material was obtained for histological examination. In the majority of these cases we still have the tissue and the sections. The ultimate results have been ascertained from time to time, the old sections restudied, and new sections made from old blocks for reinvestigation.

It is upon the evidence of this investigation, which has been going on for more than five years, on material collected for more than twenty years, that the statement can be made that the number of cures of cancer can be increased.

BENIGN PIGMENTED MOLES. This is rather a distinct type of tumor, clinically and histologically. The mole is undoubtedly of embryonic origin; whether the cells are of epiblastic or mesoblastic source makes practically little difference. For years physicians and surgeons have been familiar with the malignant tumor which may develop in one of these innocent moles at any time of life, usually late—after forty years. In the past, surgeons have again and again operated for the malignant development, or at least for what they considered malignant change; that is, local growth in the mole with slight ulceration. After such operations the patient usually returned with metastases and was sometimes subjected to operation again. Due to the unfortunate fact that, until recently, careful investigation of the ultimate results were not made, the hopelessness of this malignant pigmented mole has only been appreciated in recent years. The writer has records of 68 cases; in 43 of these there is no question but that the malignant tumor developed in a congenital pigmented mole; in the remaining 25 cases the patient was unaware of a congenital mole, but had observed a mole, not at all different from a congenital mole, months or years before the beginning of the symptoms of the malignant growth. In this group of patients there is but one which may be considered as a possible cure. The specimens in this case were sent to me by Dr. Wainwright, of Scranton, Pa., and there can be no doubt as to the clinical and pathological malignancy. In addition to the operation for the primary tumor, two operations were performed for metastatic tumors. Microscopically, the three pieces of tissue show the typical pigmented alveolar tumor, which I prefer to call malignant pigmented mole.

During this same time we have records in the laboratory of 175 benign pigmented moles, the majority congenital, some first ob-

served later in life. In the beginning of the history of this clinic only the larger pigmented moles were removed, so that in the first ten years of the life of our records the number of the malignant pigmented moles was greater than of the benign. In the past ten years it has been the rule to remove the benign moles whenever an opportunity was given, with the sole object of protecting the individual from the possible development of the malignant lesion which in the majority of cases is fatal.

I am unable to find among the benign pigmented moles so removed a single instance of later malignancy, in the scar or elsewhere. This shows that the histological examinations and diagnoses combined with the clinical picture were accurate. This shows, also, that there is no danger from the excision of a benign pigmented mole. However, again and again, when I have discussed this in public addresses, some one or more present have made the statement that it is dangerous to cut out a pigmented mole; that there is usually local recurrence in the scar; and not infrequently secondary development of malignancy. I have never observed such a result in any of our cases where the excision had been complete.

Here, therefore, is a pure clinical and pathological investigation, a complete record of the disease demonstrating that the number of cures of the malignant pigmented mole can be increased only by educating the people and the profession to the possible potential dangers of the benign pigmented mole. A chapter could be written on what moles should always be removed and on the more dangerous situations, but this is not the place for this presentation. We require no better proof of the value of a painstaking and accurate investigation of the ultimate results in a large number of cases of a single type of malignant tumor and its benign prototype.

BENIGN CONNECTIVE-TISSUE TUMORS. I have for comparison 406 cases of benign connective-tissue tumors of the skin and subcutaneous tissue with 132 examples of sarcoma. This shows that the probability of malignancy is at least 25 per cent. It is quite true that patients suffering with the different types of benign connective-tissue tumors, who have delayed treatment for months or years, have not suffered, except in rare instances, for this delay. It may, however, be stated emphatically that every one of these patients ran the risk of sarcoma developing in the benign tumor. These benign connective-tissue lesions are visible and palpable. In many cases the diagnosis is positive from the clinical picture only—for example, in hemangioma of the skin. Others are subcutaneous masses, and their nature can only be suspected. In the past, both surgeons and physicians have viewed these benign connective-tissue tumors lightly, and unless the patients have sought advice on account of the increasing size and discomfort of the tumor, operations have not been advised. During the

same time surgeons have been operating upon and saving very few sarcomas. The writer does not know whether they have realized the high mortality of sarcoma of the skin and soft parts, or that when these cases of sarcoma come under their observation the tumor had usually been present a year or more, and that in the beginning the lesion, with great probability, had been one of the various types of benign connective-tissue tumors.

The second neglected clinical fact is trauma. The swelling so common after contusions receives little attention, unless it causes great pain. A swelling which does not disappear after a certain time, or which reappears after a certain period, is a significant clinical phenomenon usually not appreciated until too late, when sarcoma has become clinically evident, and the probability of a cure least. The number of inoperable cases is large.

The following figures in regard to sarcoma of the skin and soft parts illustrate these points.

SARCOMA OF THE SKIN. In 6 cases the perithelial angiosarcoma developed in a congenital nevus. The local growth in the nevus had been present for years in all cases before the patient sought operative help. There had been an opportunity in every case to excise the congenital nevus locally the moment these local changes took place. Among these 6 cases only 1 cure is recorded.

In 8 cases of sarcoma of the skin the tumors, macroscopically and microscopically, could not be differentiated from the 6 cases of perithelial angiosarcoma which developed in congenital nevi. In 5 of these cases the tumor had been present one or more years in only 3 cases less than a year. In every instance, therefore, there had been an opportunity for an earlier complete local operation. Not one of these 8 cases was cured.

The writer has records of 95 cases of hemangioma of the skin and subcutaneous tissue; 15 fibroangiomas; 13 granulation-tissue tumors; 9 intermuscular angiomas—132 benign tumors, therefore, as compared with 14 sarcomas of the skin. These 132 patients with benign angiomas had, as a matter of fact, nothing to gain by delay. The probability of malignant degeneration is comparatively slight, but the probability of mutilating growth is so great that there is every reason not to delay in the treatment of an angioma.

20 cases of sarcoma of the skin developed in scars. In this group there are 8 cures; 7 patients, we know, are not cured; 5 patients have been lost track of. In every one of these cases the growth in the scar had continued one or more years, so that in every case there was sufficient clinical indication for an earlier intervention. Now, if the probability of a cure be 50 per cent. in late intervention, we can be quite sure that it will be much greater in early intervention. These scar-tissue sarcomas are entirely different local growths from the benign keloids, of which we have 49 examples.

We cannot enter here into a discussion of the difference between the benign keloid and the other fibrous growth in scar tissue, which is more dangerous. The malignant tumor is more apt to develop in the scar the seat of an ulcer.

In 9 cases of sarcoma of the skin there was a distinct history of a fibroma: 5 of these cases have been cured; 3 we know were not cured, but died of metastatic sarcoma. In every instance the original tumor—the fibroma—had been present one or more years. The clinical changes which suggested malignancy were rapid growth, infiltration of the covering skin or epidermis, and superficial ulceration. One, however, cannot prognosticate from this local growth the malignancy of the tumor. One of the cured cases was clinically most malignant, one of the cases which died of metastasis least so.

During the same time we have records of 67 cases of benign fibromas: 20 of these were situated on tendon sheaths, 13 in the abdominal wall, and 34 were either subepidermal or subcutaneous. From these figures, therefore, the probability of malignant degeneration in a fibroma was 13 per cent.

As far as we know multiple sarcoma of the skin and mycosis fungoides are incurable diseases, but the precancerous lesion of the skin, whether it be of epithelial or connective-tissue origin, is so distinct that our future statistics should show a great decrease in the number of malignant tumors and a correspondingly greater increase in the number of the precancerous benign lesions. I feel that a patient with a sarcoma in a scar or in a fibroma should always be treated in time for a cure. The rapid development of some of the perithelial angiosarcomas of the skin shows the danger of even a short delay. For example, in this group there are 3 tumors of the scalp, single tumors which clinically could not be distinguished from benign wens. Yet, after their removal, they proved to be sarcoma, and the patients died of metastases.

SARCOMA OF THE SOFT PARTS. The proof of a distinct precancerous lesion in this group is more difficult, but in the great majority of cases some palpable lesion had been present at least a year—long enough, therefore, to justify exploration.

In the fibrospindle-celled tumors, which resemble sarcoma of the skin developing in a scar or fibroma, we have but 3 cures among 8 cases; in only 3 of these cases had the lesion been present less than one year.

The fibromyxosarcoma of nerve sheaths is a distinct clinical and histological lesion. They may be single or multiple. In many instances the little tumor is observed at birth, in others it appears later in life. Our records show 32 examples of benign fibromyxomas of the nerve sheaths; in 9 instances the lesion was multiple; in 11 cases the removed tumor was in places histologically sarcoma; in 3 of these cases the patients had multiple tumors, one of which,

however, showed growth and malignancy. Of the 9 traced cases only 4—less than 50 per cent, have remained well; 5 patients died of local recurrence or internal metastasis. In 9 of these 11 malignant cases the tumors had been present one year or more.

The remaining cases of sarcoma of the soft parts belong to the most malignant type. There are 63 cases in all: 11, or 17 per cent., were inoperable. In not a single one of these 63 cases was the palpable mass subjected to operation within one month. In 34 cases the tumors were present one year or more; in 29 cases one month to one year. Among these 63 cases there were but 5 cures. The failure to cure was due in many instances not to the extent of the local growth but to metastases. Many of these patients gave a history of trauma previous to the appearance of the lump. Five cures are less than 8 per cent. These tumors were all cellular sarcomas of different types. Among the 10 cases of endothelioma there were two which developed in subcutaneous tumors, these had been present ten and twenty years. These little, innocent, compressible, palpable nodules could have been easily removed during the years of quiescence.

Few in the profession know how relatively few the cures are in sarcoma. Here we have 84 cases of the skin and soft parts with but 13 cures, or 15 per cent.; in the less malignant type 21 cases with 9 cures, or 42 per cent.; in the more malignant type, 63 cases with 5 cures, or less than 8 per cent.

There is no way to increase the number of cures in this type of malignant tumor except by educating the people and ourselves to the radical removal of skin and subcutaneous nodules the moment they appear. Such operations need never be mutilating nor dangerous. Intervention for the swelling after a trauma must also be resorted to early.

These, therefore, are our statistics of benign and connective-tissue tumors which indicate what a clinical investigation can do toward the improvement of the results in the treatment of malignant disease.

EPITHELIAL TUMORS. Here we have for study 977 cases of epithelial tumors of the skin and visible mucous membrane which have been subdivided into the following localizations: lower and upper lip, face, chin, eyelid, ear, nose, scalp, mucous membrane of the gum and mouth, tonsil and pharynx, larynx, tongue and floor of the mouth, skin of the neck, branchial cleft cancer, skin of the upper and lower extremities, penis and body. In every one of these cases the cancer had developed in a preëxisting lesion. Up to the present time only 173 individuals presented themselves for treatment with benign lesions, or 17 per cent. We have been unable to find a single local recurrence or death from cancer in this group. The benign lesions had been warts of various types, areas of keratosis of various types, and benign ulcers. It is inter-

esting to note that the number of these benign lesions applying for treatment are on the increase. Up until 1910 the percentage of these was but 14, in the past two years the benign precancerous lesions have increased to 39 per cent., and the relative number of fully developed cancer is apparently on the decrease. Of course, this is difficult to estimate with any degree of accuracy until the difference is more marked; 69 cases, or 8 per cent., came under treatment as warts, that is, clinically benign lesions; but when studied microscopically they proved to be malignant. In this group up to the present time we have been able to find but one failure to cure. In this case the warty growth on the lower lip extended almost from angle to angle of the mouth, and we feel convinced that it was incompletely removed. The failure to cure, therefore, was due to the operation. In the remaining cases the skin lesion was fully developed carcinoma. We mean by this in the gross an ulcer or a fungus, and microscopically a carcinoma. We can recognize three distinct types: the *basocellular carcinoma*, 19 per cent. of the total cases, with the probability of a cure in 70 per cent. from our experience; this includes all cases—inoperable, extensive, and recurrent. The *carcinoma spinocellulare* is the most frequent type of cancer. The large number of this type of cancer is due to its common occurrence on the lower lip and tongue, and here the spinocellular cancer predominates. Considering all cases, the percentage of cures in this group is 40. There is a third type of carcinoma of the skin and mucous membranes, one in which the tumor is composed of transitional epithelial cells. Krompecher employs for this form the term *carcinoma cubocellulare*. These cases represent but 5 per cent. of the total, and the percentage of cures is 33.

In an experience, therefore, of more than twenty years with 820 cases of malignant tumors of the skin and mucous membranes, the percentage of cures varies from 33 to 98 in the four types of cancer. We feel certain that this number of cures should be greatly increased, in some localizations, to even 100 per cent.

My table shows that between the years 1890 and 1913, 16 patients have sought advice with lesions of less than one month's duration. (Practically all of these are recent cases, and in people who have been reached directly by the education of the students of the third and fourth year.) Fifty patients sought advice within two months after the onset of the first lesion; 77 between three and six months; 109 between six and twelve months; 344 one to ten years or more. In many cases we have no exact data.

In epithelial tumors the danger of delay after the first symptoms varies with the character of the lesion and its localization. In some localizations one day's delay is equal to a week in another, a month in still another, and a year in still others. The danger of delay is greatest in the spinocellular tumors and in localizations, such as the lower lip and tongue.

It is hoped that these statistical figures of clinical, pathological, and ultimate-result records will prove that the number of cures of cancer will be greatly increased by the proper excision of the precancerous lesion or of the malignant lesion in its earlier stage, and there is no reason why this should not be done. No one is ignorant of the lesion in its early days, they are only ignorant of its potential dangers. To cut out with the knife these lesions in their earliest stages is not major surgery, but it is delicate surgery. The surgery presents no danger, rarely much discomfort, and seldom even slight mutilation. But the surgeon must know how to cut out these lesions. To leave a piece of the benign wart, or of any other type of precancerous lesion behind, is to leave a focus more dangerous than the entire focus uninjured. To incompletely cut out cancer in its earlier stages gives worse results than a complete eradication later.

The danger of excision of the precancerous or early malignant lesion is due to the fact that the surgeon may make his operation less complete because of the innocent appearance of the lesion. There is absolutely no necessity for this. In some cases, especially in the early malignant stage, the Paquelin or electric cautery, or fulguration, may be employed with or without the knife, but a piece of the lesion should always be obtained for microscopic record. Otherwise we will have no check and no accurate knowledge of what we are treating. In a few cases the clinical evidence of malignancy is so obvious, the danger of cutting out a piece so great, and the situation of the lesion so convenient for cautery or fulguration, that we treat the disease without microscopic proof. But this is a strictly surgical problem.

We are also confident that we shall be able to show in a future article that the number of cures of cancer in the later stages can be increased by better surgery.

We have discussed here the problem of lesions of the breast, of the jaws, thyroid and salivary glands, the stomach, gall-bladder, colon, or rectum, but here too our material and the clinical, pathological, and ultimate-result records will show that the number of cures of cancer will be greatly increased by the proper excision of the precancerous lesion or early cancerous stage, and that better surgery will increase the number of cures even in the later stages of cancer.

Surgery at the present time offers more for the cure of cancer than any other method of treatment, and is doing more today than merely treating cases of cancer as they apply for help. Surgeons are collecting these statistics, by which they hope to educate the people that incurable cancer is, in the great majority of cases, a preventable disease. All that patients are asked to do is to submit to an operation in the beginning of the trouble, and this operation should excite no fear or anxiety.

NOTE.—Since this paper was written, the results in all the cases of carcinoma and sarcoma have been again ascertained during the past summer. I will give here the results, as roughly computed, in the cases of cancer of the tongue, lip, and breast. These results add confirmation to the evidence already offered—that it can be proved from clinical and pathological records that the number of cures of cancer will be greatly increased by the proper excision in the earliest precancerous and cancerous stage of the local disease. These figures are based on cases recorded in the surgical pathological laboratory of the Johns Hopkins Hospital. Most of the tissues and records in these cases have come from the clinic of Prof. Halsted, of the Johns Hopkins Hospital, but many have been received from the Union Protestant and St. Agnes' Hospitals and elsewhere. During the years 1889 to 1908, almost twenty years, we have accumulated in the laboratory records of 70 cases of cancer of the tongue. In the last five years we observed 30 cases. During the past five years much emphasis has been placed upon the precancerous lesion and the early recognition and treatment of the malignant lesion. The results of this education of the students is shown in the great change in the character of cases of cancer of the tongue. In the first period there were 6, or 23 per cent., of precancerous benign lesions; in the last period, 9 cases, or 33 per cent. In the first period the percentage of inoperable cases was 18, or in the last period this has been reduced to 10 per cent. The cures in cases of undoubted cancer during the first period was but 21 per cent. (5 cured cases). In the last period 6 cases, or 50 per cent., are free from any evidence of recurrence today. The usual time of recurrence after operation for cancer of the tongue is less than nine months, and in all of these cases, recorded as cured, a period of at least nine months had elapsed since operation. This increase in the percentage of cured cases is due, I believe, to the fact that the patients have sought advice earlier; some of the better results may be attributed to better surgery. Here, therefore, we have rather startling figures; precancerous lesions increase from 23 to 33 per cent; very late inoperable cases drop from 18 to 10 per cent; operative cures increase from 21 to 50 per cent.

Cancer of the Breast. During the first period up until 1908 the inoperable cases of cancer of the breast were 27.5 per cent. which has in the past five years fallen to 18 per cent. The percentage of five-year cures up to 1908 was 35 and up to 1913, 42. The difference between early and late intervention is shown by the following figures: In those cases of cancer of the breast in which the diagnosis could not be made clinically, but was made after exploration of the lump, the percentage of five-year cures has varied from 85 to 100. In adenocarcinoma, the least malignant form of carcinoma of the breast, there are 15 cases, all of

which have remained well since operation. In the more malignant types of cancer of the breast subjected to operation in this early period there have been 12 five-year cures, or 85 per cent. We have called this group of cases of cancer of the breast "clinically benign." There has been found at the examination only a palpable lump; there were no changes in the nipple or skin which could be looked upon as signs of malignancy. In gross appearance and under the microscope these clinically benign cases of cancer do not differ from those in the second group called "clinically malignant." The difference between these groups is *clinical only*. In the clinically malignant group the diagnosis of cancer was made from the infiltration of the tumor associated with changes in the nipple and skin. The disease in this group was undoubtedly in a later stage. The difference in the results is startling. In adenocarcinoma the percentage of cures in the benign group is 100; with the same cancer clinically malignant it is but 64. That is, a woman whose lump is an adenocarcinoma, if she delay until the diagnosis of cancer can be made clinically, reduces the probability of her cure from 100 to 64 per cent. In the more malignant types of cancer the probability of a cure is reduced from 85 to 33 per cent.

After a most careful investigation of all the facts available from about 1300 cases of tumors of the breast, we may formulate the following conclusions: If every woman over twenty-five years of age were to seek surgical advice the moment she felt a lump in the breast and the surgeon explored this lump at once, the probabilities are that the lump would prove to be benign in about 33 per cent. of cases; in the malignant cases the chances are that the tumor would be adenocarcinoma in 20 per cent. of the cases, with the probability of a cure of 100 per cent. If the lump represented the most malignant forms of cancer, the chances are 85 per cent. of a cure. Now, with the same *good* surgery, these figures should improve as the number of early cases increases. For undoubtedly many cases of cancer subjected to operative treatment late had been distinctly benign lumps for months or even years. The danger of incomplete surgery in the early stage of cancer has been fully discussed in another publication.²

Carcinoma of the Lip. In about 200 recorded cases I find that the benign precancerous lesions have increased tremendously, especially in the past two years. Of 12 cases which must be looked upon as distinctly benign and in which two years or more have elapsed since operation, there has not been a single failure to cure. In a group of 16 cases which may be looked upon as early cancer (malignant warts) there has been but one failure to cure, that is, the percentage of cures is about 96. In this case the local lesion,

² Jour. Amer. Med. Assoc., September 20, 1913, lxi, 911.

the malignant wart, involved almost the entire lower lip. There was a local recurrence due, I believe, to incomplete excision. The percentage of inoperable cases is also diminishing. When we consider the fully developed carcinoma of the lip in which five years or more have elapsed since operation, we have the following figures:

Group 1. Excision of lesion on lip only 7 cures, or 63 per cent. The failure to cure in 4 cases was due to metastasis to the glands beneath the jaw.

Group 2. Excision of lesion on lip and of the glands beneath jaw. In the cases in which the glands removed showed no evidence of metastasis there have been 20 cures, or 95 per cent. The one failure to cure was due to a local recurrence on the lip (again, probably, incomplete surgery). When the glands removed showed metastasis under the microscope the percentage of cures falls to 50 (6 cases.) These figures, therefore, show that if men will subject themselves to proper surgical treatment for those lesions which precede cancer their chances of a cure should be 100 per cent. Even in the early stage of cancer the proper excision of the local growth on the lip and removal of the glands of the neck should offer almost 100 per cent. Delay, however, with its increasing chances of metastasis to the glands diminishes the probability of a cure.

UNUSUAL TYPE OF ACID INTOXICATION IN INFANTS.

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THE term "acid intoxication" has been used somewhat loosely. In infancy and childhood it is produced under varying clinical conditions. It is generally agreed, as was shown by Langstein and Meyer,¹ that acetone in small quantities may occur in the urine of normal children. Acid intoxication results from incomplete fat and protein metabolism, due to functional or organic diseases of the liver or to carbohydrate starvation. It is generally believed that carbohydrate is an important factor in fat and protein metabolism. If the carbohydrate be absent, it is thought that oxidation is imperfect and beta-oxybutyric acid is formed. Beta-oxybutyric acid is not readily demonstrated in the urine, but this acid is further oxidized into diacetic acid and acetone. The presence of acetone is used as a clinical index for the demonstration of acidosis. Mellanby² and Sedgwick³ have shown that

¹ Jahrb. f. Kinderheilk., 1905, lxi, 454.

² Lancet, London, 1911, clxxxi, 8.

³ Amer. Jour. Dis. Child., April, 1912, 209.

creatin and creatinin are excreted in increased amounts during recurrent vomiting attacks. Cathcart⁴ found that creatin is constantly present in the urine during starvation, and that carbohydrates given after fasting decrease the creatin, whereas fats given after the starvation increase the creatin. It is, therefore, shown that carbohydrates are required in normal protein metabolism, and also that the elimination of creatin and acetone is produced by similar diets. It is not proved that the production of abnormal acids of the oxybutyric series is without toxic effect. Even though we agree that they are not the primary cause of the condition, nevertheless, they may exert a secondary influence as the result of carbohydrate starvation, whether from persistent vomiting or carbohydrate-poor diet.

A. Loeb⁵ recently called attention to the probable toxic effect caused by the administration of acetic acid. He showed that its use may cause acidosis or ketonuria.

It is found that acetone and diacetic acid are present under a variety of clinical conditions. In the infectious diseases acetonuria persists in spite of a considerable carbohydrate ingestion, probably due to some basic alteration in metabolism. Considerable acetone is found in the urine of children who are recovering from chloroform narcosis. Acetone also occurs in some gastro-intestinal disturbances of children not suffering from inanition. The acidosis of "recurrent vomiting" cannot be explained entirely on the basis of starvation. Acid intoxication results after certain forms of poisoning; phosphorus, which produces tissue necrosis in the liver, is capable of causing most marked acetonuria. Similarly, atropin, morphine, lead, and antipyrin may cause acidosis.

In the acute infectious diseases, particularly diphtheria, scarlet fever, measles, and typhoid, in prolonged starvation from any cause; also in diabetes and malignant disease, marked increase in the production of acetone occurs. Else Liefmann⁶ has recently published a report on the occurrence of acetone in children suffering from spasmophilia, in which she attempts to show that the elimination of acetone is constantly increased.

The object of this paper is to call attention to a series of cases which have come under my observation during the past several years. They were severe types of acid intoxication, and usually terminated fatally. They occurred mostly in previously healthy infants at about the weaning period. In most instances the infants came from healthy parents. In one family two children had died from this affection. The third child, whose history will be given below, was similarly attacked, but recovered after a severe illness. Dr. Wesley F. Orr, of Idaho,⁷ reports five children

⁴ Jour. Physiol., 1909, xxxix, 311.

⁶ Jahrb. f. Kinderheilk., Band lxxvii, Heft 2.

⁵ Bio. Chem. Zeitschr., 1912, xlvii, 118.

⁷ Personal Communication.

in the same family who died with symptoms similar to those which we are about to describe. These cases led us to believe that there is a familial type of the disorder.

CHARACTERISTICS OF THE DISEASE. The illness usually occurs in large, robust, previously healthy infants. In some cases the children show a stationary weight curve for several weeks before the onset. If fed at the breast, they show signs of hunger and dissatisfaction with the food because the breast milk is scanty or of poor quality. Some of the infants in this series were artificially fed for weeks or months before the onset of the illness.

The disease is ushered in by gastro-intestinal symptoms, consisting of more or less diarrhea, and nearly always vomiting. The patients are at first restless and show moderate febrile reaction during the first days of the illness, rarely exceeding 101° . Later on the temperature tends to be lower, averaging between 99° and 100° . On the second or third days there is some abdominal distention, dyspnea, with rapid respiration and an increase in pulse-rate. The respirations are labored, and the accessory muscles of respiration show marked activity. The liver is markedly enlarged, the edges are plump, and the surface firm. The urine soon contains albumin, and hyalin and granular casts, without blood, with acetone and diacetic acid. In one of my cases leucin and tyrosin were also found. The urine contains no sugar.

About the third day stupor is noted, which gradually deepens into coma. The blood shows no pathological changes, the leukocytes vary between 9000 and 12,000, and the differential count shows no variation from normal. Toward the close of the disease intestinal atony may occur. As a result, no feces or gas are passed voluntarily, nor can any intestinal evacuation be induced by mechanical or therapeutic agents. Abdominal distention increases progressively, and cyanosis and dyspnea are marked. Unconsciousness continues, and occasionally vomiting persists until the end. The reflexes are present and normal. There are no symptoms of cranial nerve involvement, and usually no pulmonary complications. When death takes place it usually occurs in four or five days after the onset.

I shall report several typical cases from my clinical records. I have notes on nine cases, not including the severer types of cyclic vomiting, with the presence of large quantities of acetone and diacetic acid. In passing, I may say that a typical case of cyclic vomiting occurring in my practice proved fatal, though such cases are not included in this report.

The first case of this unusual type of acid intoxication came under my observation September 1, 1902.

CASE I.—The patient was one year old; the father was a physician. On August 30, after the infant had been nursed, she was taken seriously ill with vomiting. She vomited several times

during the night: First food, and later on a clear watery fluid. The father administered one grain of calomel in divided doses and other mild laxatives. The child's bowels moved the next day, and she passed gas, though the vomiting continued. On September 2 the following notes were made: Well-nourished female child; slight evidence of rickets; some roughness of the respiratory note over the right upper lobe. Respirations rapid; pulse full, strong, moderately accelerated. Temperature, 99.5° F. Examination of the head, mouth, pharynx, and glandular system of the neck proved negative. The liver was enlarged and felt doughy; abdomen flat; spleen not palpable; no evidence of tumor in the abdominal cavity. There were no meningeal symptoms, though the child was inclined to be stuporous. The following day it was noted that the child was obstinately constipated; the vomiting continued and the abdomen had become slightly tympanitic. The expiratory note in the right upper lobe was an exaggerated vesicular type, though there was no dulness on percussion. On observation it was evident the child suffered from abdominal pain. She was inclined to sleep, though she could be aroused. It is worthy of note that while the temperature was low the pulse was of good quality, though accelerated, and the respirations were extremely rapid, somewhat noisy, and superficial. Later in the evening it was thought that the child passed gas, though there had been no fecal evacuation during the day. She had been given a simple, non-irritating diet. Water was vomited shortly after being given. On the morning of the fifth day the patient developed alarming symptoms, and the father sought the advice of a neighboring physician. The child had not evacuated its bowels for twenty-four hours, and because no gas had been passed, the physician who was summoned concluded that the primary difficulty was a mechanical obstruction of the intestines, and surgical consultation was called. At this consultation the opinion was expressed that the child was suffering from intussusception. This later proved to be incorrect. The following morning the infant's respirations were rapid, pulse feeble, abdomen tympanitic, and the child was plainly in collapse. The urinary examination showed acetone and diacetic acid, a trace of albumin with casts, and an evaporated specimen showed leucin and tyrosin. During the day the child grew progressively worse; stimulation was employed without effect. A careful abdominal and rectal examination gave no evidence of intussusception, nor any other form of mechanical obstruction of the bowel. Crepitant rales were heard over the right upper thorax.

September 4. The child died at 7 P.M.

September 5. Autopsy was performed, with the following findings: The abdomen contained no free fluid; the peritoneum was smooth, shining, and somewhat injected. The great omentum and

the mesenteric glands were normal. A systematic examination of the bowel showed no adhesions or inflammatory reaction in the mesentery or in the serosa covering the bowel; no intestinal obstruction of any kind or nature; mesenteric glands were not enlarged. The spleen was about normal in size, and presented no pathological change. The liver was striking, because it was markedly increased in size, and presented a light yellowish terra-cotta appearance.

The liver on section showed that the surface was glistening, decidedly yellow, and the knife was greasy because of the fatty nature of the tissues.

The capsule of the kidney stripped readily. The cortical markings were obliterated; turbid urine exuded from the pelvis. There was no vascular engorgement, though fatty changes were present.

In the intestine an occasional Peyer's patch stood out prominently, and was the site of an inflammatory reaction.

The lungs showed small areas of focal inflammation and congestion at the bases.

The heart muscle was light in color, though it was well contracted. The valves were normal.

The histological study was made by the late Dr. Howard T. Ricketts. His report is briefly abstracted herewith: A study of the liver showed that the markings of the lobules were not distinct. There was no increase in the connective tissue of the liver. The liver cells stained poorly. Fatty degeneration of the parenchymatous cells was extreme and widespread, being more marked in the periphery of the lobules than in their centres. Little protoplasm was left in such cells, and what remained was granular. The centre of the lobules showed marked granular degeneration. There were also many small areas where neither the nucleus nor the cell body was stained; no normal liver tissue was seen. Many large bacilli not staining by Gram were present, but had no distinctive distribution. In the lungs the vessels were congested. There were certain areas in which the air cells were filled with red-blood corpuscles, though there were a few leukocytes among the extravasated red cells. Moderate fatty degeneration was found here and there in the parenchyma of the kidneys. There were no hemorrhages.

Summarizing the histological findings one notes:

Heart: Moderate focal necrosis.

Lung: Acute hemorrhagic lobular pneumonia (*Diplococcus pneumoniae*, probably). Moderate necrosis of epithelial cells. General pulmonary congestion.

Liver: Extensive granular and fatty degeneration, the picture resembling acute phosphorus poisoning.

Kidney: Acute granular and fatty degeneration of the parenchymatous tissue.

In my series of nine cases four autopsies were performed, with findings like those described above, the predominating feature being fatty degeneration of the liver and other organs.

CASE II.—A male child, aged one year, who had been previously weaned and was receiving artificial food, entered the hospital August 1, 1911. He was taken sick three days previously, suffering from moderate diarrhea, having three to five stools daily. The baby vomited several times after nursing. A slight fever was observed during the first day of the disease. He had been restless, cried much of the time, and suffered from abdominal distention. On the third day of the illness he developed a mild stupor. The mother becoming alarmed, sought the hospital. On admission it was noted that the baby was well-developed, well-nourished, and was breathing rapidly and superficially; pulse, 172; respirations, 49; temperature, 101.4° F. Examination of the heart and lungs was negative. The liver was distinctly enlarged; the spleen was not palpable; the abdomen was moderately distended. In a short time the temperature was found to be 99°, pulse 160, and respirations 40. The urine was acid, contained a faint trace of albumin, no sugar, though a marked quantity of acetone and diacetic acid, an occasional leukocyte, but no red cells. The baby died twelve hours after admission to the hospital. No autopsy was permitted.

CASE III.—On October 2, 1911, a physician brought his child to us from a neighboring city. A male child, eleven months old, had made phenomenal gain in weight. At seven months of age he weighed twenty pounds. After the seventh month he remained stationary in weight. For the past three weeks the patient had been unable to satisfy his hunger at the breast. He was nursed every hour to every hour and a half, whereas previously he had been nursed every three hours. The mother noted that her breast milk had been scarce, and that she herself had lost in weight during the past several weeks. Four days before admission to the hospital he was weaned from the breast. He refused all nourishment and took only water. For the next few days he took little or no food. The bowel movements were regular, and he urinated frequently. On October 1, he became constipated, and had no bowel movement; previously he had two or three evacuations a day. October 2, he started to show signs of dyspnea, the respirations became rapid, and later in the day he became stuporous, with a pulse of 140. Constipation persisted, and he continued to refuse all kinds of food except water, which he desired at frequent intervals. He vomited every three or four hours. The examination was for the most part negative; the abdomen was slightly distended; the liver extended three fingers' breadth below the costal arch, and seemed doughy on palpation. The urine contained albumin, hyalin and granular casts, and acetone and diacetic acid in abundance. He succeeded in having several bowel movements on the day of admission, and expelled some flatus. The treatment consisted of the administration of sodium bicarbonate solution by mouth; atropin, grain $\frac{1}{1000}$ by mouth; twenty drops

of brandy, repeated at short intervals; and strained oatmeal gruel was used as food. In addition to the above a solution of sodium bicarbonate was given subcutancoulsy, and 8 per cent. of glucose in normal salt solution was given by rectum, using the drop method. He died October 3, at 1.45 P.M. No autopsy was permitted.

CASE IV.—H. B. T., male child, aged six months; was born normally; weighed eight pounds; gained steadily in weight; erupted first teeth at four months; had six teeth at six months, and sat erect. Was a large, strong, robust child; had mother's milk exclusively since birth. Was somewhat colicky during the first month of life, and since four weeks of age had been nursed five times in twenty-four hours. No other foods were given; no fruit or vegetable juices. He never had a sick day until the onset of the present illness. Three days before the admission to the hospital he weighed twenty pounds and four ounces, having gained five ounces in the past week. The bowels moved once or twice a day, and the movements were normal. The baby always slept well and showed no urinary symptoms. On the first day of the illness the stool contained mucus, and was of a greenish color, though the infant appeared as well as usual. The next day the infant again had two bright green stools, though he appeared well. The third day the infant had another greenish stool, but since that time (twenty-four hours) had had no bowel movement. Cried at intervals, and seemed restless and uncomfortable. At 6 A.M., September 26, 1912, it was noted that the child began to breathe rapidly and heavily, became languid and drowsy, passed very little urine, and bowels became obstinately constipated. He became cyanosed, had a drawn expression of the face; slight fever, 99° F.; pulse, 120.

The Family History. The father suffered from headache since boyhood; the father's mother had had headaches; the father's father died from alcoholism; a brother was epileptic. The mother stated that her health was perfect in every way: no chronic disease and no tuberculosis. The mother's sister has a goitre. Her parents are living and well. The patient has a sister, five years old, who has always enjoyed good health. Two children in this family died from a condition resembling the present attack of the patient. The first child lived eleven months, was being weaned, and was having a few bottles of cows' milk daily in addition to breast feeding. The baby had been on mixed feedings for three weeks, when he showed signs of indigestion, with greenish stools, though he was not severely ill. After persisting three or four days the patient suddenly was seized with rapid breathing, followed by stupor, and he died in forty-eight hours. The second child, a boy, aged nine months, very large and well-developed; died eighteen months previously; he was fed at the breast, and was given one bottle a day. This feeding had gone on for three or four weeks. At the

expiration of this time he showed signs of indigestion, with greenish, mucous stools, and within a few days began to breathe rapidly, was stuporous, bowels were constipated, and on the fourth day he went into coma, and remained comatose until death, which occurred on the sixth day.

The third baby of this family, the subject of this clinical record, was admitted to the hospital on September 26, 1912; temperature, 101° F.; pulse, 120; respirations, 36. The respirations were rapid and superficial; the infant was cyanosed. The general examination of the head and thorax was negative. The liver was enlarged, though the spleen was not palpable. The reflexes were all somewhat exaggerated. The skin showed a peculiar, pasty appearance. There was no edema. The stools were slightly increased in frequency, greenish and watery, and of a peculiar, penetrating, sour odor. The child was irritable and restless at times, and often fell into a profound sleep. In order that I might study the condition accurately, the mother's urine was collected, and her breast milk was subjected to various examinations. Examination of the *mother's* urine made on the first day of admission to the hospital showed: specific gravity, 1.030; faint trace of albumin; 0.7 per cent. sugar; trace of acetone; no diacetic acid; a few epithelial cells; a few leukocytes; no casts; the fermentation test for sugar was negative. The *infant's* urine, examined about the same time, showed a faint trace of albumin; no sugar; acetone and diacetic acid; ammonia, 0.0952 per cent. Upon testing the baby's urine with the polariscope and by chemical methods no sugar was present. The sugar rapidly disappeared from the mother's urine. A tolerance test for sugar in the mother was made by the ingestion of 140 grams of sugar; urine taken two and four hours afterward showed no sugar by Fehling's test or the polariscope.

For the next few days the infant was extremely ill: showed abdominal distention, vomited occasionally, and had a tendency to be drowsy. On October 1, he became much worse: respirations were increased; pulse small and intermittent; on account of what seemed a *disastrous* collapse, he was given a 2 per cent. solution of sodium bicarbonate subcutaneously in the interscapular region. An examination of the urine at this time showed that it was alkaline, with a marked acetone and diacetic acid reactions. After a precarious night the baby seemed better, next morning, though the area where the subcutaneous injection had been given showed a marked tendency to gangrene and sloughing. The following day the baby presented general edema; puffiness of the face and scrotum; the skin everywhere edematous; no albumin in the urine; and the acetone and diacetic acid were markedly less.

The mother's milk showed 5.5 per cent. of fat; no acetone or diacetic acid. The breast milk was fed to a kitten, and was injected subcutaneously into guinea-pigs and rabbits without in any case

producing the slightest toxic effect. No acetone or diacetic acid was recovered from any of the animals that were tested. After ten days of severe illness the edema disappeared, the patient gradually became playful and happy, and except for the large slough between the scapulæ, was perfectly comfortable.

The treatment consisted of weaning the baby from the breast milk, giving rectal infusions of 8 per cent. glucose in normal salt solution, large doses of sodium bicarbonate by mouth, of whisky, or sour wine in half-dram doses every two hours; powdered casein in half-dram doses in oatmeal-gruel every two hours; soy-bean soup three times a day; occasional oxygen inhalations when cyanosis and dyspnea were most marked; and the subcutaneous infusion of sodium bicarbonate. Two per cent. levulose and sodium bicarbonate were given by mouth. The patient made a complete recovery, and has progressed up to the present time, with an occasional upset. The mother makes almost daily examination of the urine, testing for acetone and diacetic acid, and on one or two occasions has discovered the faintest trace. Aside from this the patient has remained well up to the present time.

The interesting points about this case may be summarized as follows: Previously healthy baby was taken suddenly ill with gastro-intestinal symptoms, diarrhea, and vomiting. Enlargement of the liver followed in a few days by rapid breathing, and a marked quantity of acetone and diacetic acid in the urine. The baby showed irritability and discomfort, and at times a tendency to coma, and finally made a complete recovery.

The most striking feature of this case was the fact that two other infants of this family had previously fallen ill the same way and had died. It is noteworthy, too, that the mother showed some urinary changes upon the admission of the infant into the hospital. Though normally a calm and self-possessed woman, she was suffering from the most intense suppressed emotion because she felt that she was about to lose her third child in the same way that she had previously lost two. Possibly this may explain the glycosuria in her case. At any rate it soon disappeared, and her breast milk, which was examined chemically and injected and fed to animals, as already stated, gave no toxic reaction.

It may be thought that these cases bear a clinical identity with cases of cyclic vomiting; but in this type, vomiting is not so persistent, and sometimes scarcely occurs at all. In my series of cases of unusual acid intoxication the disease described occurs in young infants, often toward the close of lactation.

Persistent and uncontrollable emesis characterizes the cases of cyclic vomiting. Rapid, superficial breathing, enlargement of the liver, low temperature and rapid pulse, with the occurrence of tympany, obstinate constipation, with little or no vomiting toward the end, are features of the type which I am now describing.

A series of cases similar to those which I have enumerated were described by Dr. Thomas D. Parke,⁸ of Birmingham, Alabama, before the section on diseases of children at the meeting of the American Medical Association in 1907. Dr. J. Ross Snyder, of the same city, has seen the same class of cases, and has made verbal reports to me. They were mostly in infants who varied from six months to twenty months of age. Most of Parke's cases were breast-fed, though a few were artificially nourished.

In the literature one finds scant mention of this extreme form of acid intoxication in infancy. Possibly some of the severer forms have been described as cases of acute yellow atrophy of the liver, though in none of our cases was jaundice present. The liver remained constantly large, not atrophied, as in cases of acute yellow atrophy. The presence of leucin and tyrosin is not pathognomonic for acute yellow atrophy, since both substances may be found in small amounts in urine in extreme degenerative diseases of the liver, such as afebrile jaundice with slight hepatic enlargement, leukemia, typhoid fever, and other diseases.

From the urinary findings, from the symptom-complex, and from the almost universally fatal termination we are justified in assuming that some profound intoxication has taken place in the infant's organism. The symptoms which this disease group represents have suggested resemblance to the so-called "milk sickness," a condition which has been observed throughout the pioneer portions of the United States where cows became ill with the so-called "trembles," and human beings who partook of milk from such animals or ate of their flesh fell ill with a diseased condition which resembled, in some respects, the cases which we are describing. Human beings ill with this disease show languor, loss of appetite, and extreme constipation, usually marked nausea; the breath has a peculiar, sweetish odor. The pulse is quick, full and soft, and the patients have little or no temperature; drowsiness and coma are not uncommon, and irritability, convulsions, and marked delirium may occur. Notwithstanding the resemblance, those cases which we report, as well as those reported by Parke, were for the most part breast-fed infants by healthy mothers. These cases occurring frequently toward the close of the period of lactation lead us to ask whether there was some quantitative change in the breast milk sufficiently marked to produce the condition of starvation. Thus in the third case mentioned the baby had not gained weight for four months before he came under observation, and for three weeks previous to admission into the hospital he had appeared unable to satisfy his hunger while at the breast. For this reason he had been nursed every hour or hour and a half, whereas previously he had been nursed every three hours.

⁸ Jour. Amer. Med. Assoc., 1907, xlix, p. 1827.

Could a starvation acidosis have resulted, or was there some deficiency in the component parts of the breast milk which could have led to a severe intoxication?

Referring to CASE IV, (H. B. T.), the baby was plump and rotund, was receiving large quantities of breast milk, and indeed all of the infants who came under observation were well-developed, usually above the average. One would hardly conceive that these infants were in a condition of starvation, especially if they be compared with the cases of marasmus and decomposition which one so frequently sees as the result of prolonged food deprivation without any evidence of the extreme acid intoxication, or the fatty degeneration of the internal organs which we found in our series of cases. Or is the condition possibly due to a toxicity of the food *per se*? All of the animal experiments which we made showed the milk to be free from poisonous effect. It may be held that this proof is insufficient and that the small animals may have remained free from toxic symptoms, whereas the baby might have succumbed. The milk was injected in considerable quantity in guinea-pigs and rabbits and was fed to kittens. We would have expected some results if toxic products had been present. In addition, some infants, as has been pointed out, were exclusively breast-fed, while others were being artificially nourished. We conclude, therefore, that the cause did not reside in the toxicity of the food before ingestion.

Dr. Parke in his paper suggests the possibility of a bacterial origin because of the usual absence of high fever and the moderate leukocytosis. As one studies these cases he becomes impressed with the fact that the disease seems less likely to be infective or bacterial in origin than a profound metabolic disturbance. Leucin and tyrosin were found in one of our cases marked by extreme fatty degeneration of the liver. The production of these substances may be explained by the destructive cellular changes in the liver, or may be due to a breaking down of the proteids into amino-acids, and of these acids into leucin and tyrosin. In the severer cases of acute yellow atrophy these amino-acids are present in the liver as well as in the blood and in the urine, and hence leucin and tyrosin may be formed outside of the liver in other organs.

The case which recovered under treatment received considerable proteids in the form of casein, gelatin, soy-bean flour, and the animal broths, together with carbohydrates. We assumed that the patient had an intolerance for fat, consequently carbohydrates were given in abundance in the form of cooked starch and levulose. It is possible that the protein of the food was the toxic agent, though in our plan of feeding during the convalescence the protein disturbances seemed to act not unfavorably. Nor do we think that the condition should be considered in the light of an ana-

phylaxis, for many of the infants received the proteid in the form of breast milk. It may be suggested that the carbohydrate intake was insufficient to protect the fat and proteid metabolism, and possibly in this way a perversion of metabolic process occurred, so as to give rise to incomplete or toxic products, with a consequent acidosis and subsequent tissue degeneration.

Recent work has shown that toxic substances can be obtained from every protein that has been subjected to hydrolysis. This includes egg-white casein as well as bacterial proteids. Jobling and Bull⁹ have demonstrated that in bacterial proteids, probably in all porteid substances, the toxic products are found in the proteose fraction of the split products (one of the first products of protein cleavage). It has also been shown that under certain conditions the epithelial barrier of the intestines permits the large protein molecule to pass through. This has been demonstrated by the use of egg-albumen, giving rise to an alimentary albuminuria when small doses of protein were administered by mouth.

In seeking to assign a suitable cause for these unusual types of acid intoxication, it has seemed to me—from clinical experience, some experimental work, and therapeutic results—that the disease in question depends upon some derangement of the infantile metabolism, resulting in the production of toxic products from misdirected chemical processes.

The analogy based on the familial occurrence of the disorder in one of our cases leads us to note that an inherent weakness of cells or organs may exist, as in diabetes mellitus, where a marked predisposition to the disease occurs among entire families.

The cases reported by Parke, already referred to, seem identical with those contained in this report.

If I have described a disease group which has been previously classified or reported under another name, the literature has been inaccessible to me, or has not come to my notice. At any rate, the current text-books and periodic literature make no mention of these cases.

EXPERIENCE WITH NEOSALVARSAN AT THE HARLEM HOSPITAL.

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NEOSALVARSAN is now so well known that it is almost useless to burden this report with a description of its various physical

⁹ J. Ross Snyder, personal communication.

and chemical properties. I simply wish to give my experience with 175 tubes of this remedy which were kindly given to me last year by Professor Ehrlich for experimental purposes.

The work was done in the out-patient department of the Harlem Hospital, the patients being allowed to go to their homes immediately after treatment. As it had been my custom for a year or more to treat all of my salvarsan cases in an ambulatory manner, I had no hesitancy in following the same plan when using neosalvarsan. The only disadvantage in not keeping the patients in the hospital wards was that they could not be observed quite as closely. It was also impossible to record the temperatures after injections, a matter which did not seem of very vital importance.

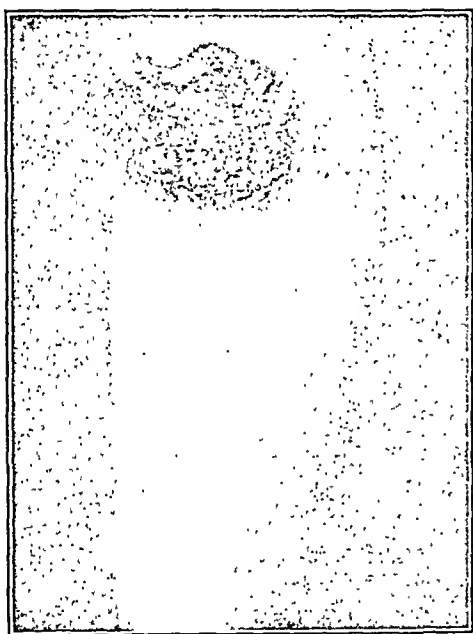


FIG. 1.—Ulcerating gumma of one year's duration.



FIG. 2.—Lesion in Fig. 1. Not entirely healed at the end of eight months after four intravenous injections of neosalvarsan.

Of the 56 patients that were treated, 45 were given intravenous injections: 1 of these received two, 17 received three, and 27 received four injections, the treatment being given as far as possible every other day. The intramuscular method was tried in 11 cases, 1 patient receiving two and the others single injections. No other antisyphilitic remedy except neosalvarsan was given.

The cases that were selected for treatment included various forms of cutaneous syphilis, mucous membrane, eye and bone lesions, a few cases of latent syphilis, and one of tabes. Macular eruptions disappeared, as a rule, within a week after treatment. Some of the papular syphilides disappeared in two to four weeks, while in one case (No. 32) the eruption was still apparent at the end of two

months. Several cases of the pustular syphilide, including one of rupial type (No. 46) responded favorably to the new remedy.

In the treatment of several cases of the nodular syphilide the result was as gratifying as that usually obtained from the use of salvarsan. In the treatment of gummas of the skin and mucous membranes the effects of the remedy varied considerably. A deep ulcerative gumma of the leg (No. 11) (Figs. 1 and 2) had not entirely healed at the end of eight months, the patient having received four intravenous injections, although an extensive nodular syphilide upon



FIG. 3.—Ulcerating gumma of one month's duration.



FIG. 4.—Same lesion as Fig. 3, three months after four intravenous injections of neosalvarsan.

another part of the body had healed promptly. A satisfactory result was obtained in a deep gummatous ulcer of the leg (No. 3), the lesion being completely healed in three months (Figs. 3 and 4).

Mucous membrane lesions showed the same tendency to rapid disappearance that is so characteristic of salvarsan. One case of condylomata, however, did not clear up until the end of five weeks, although three intravenous injections had been given. There was no objective change in a case of leukoplakia (No. 17).

The eye manifestations included one case of iridocyclitis (No. 35), which cleared up in three weeks. In another patient (No. 16) presenting a papular syphilide, an iritis occurred during the course of treatment. This appeared on the day after the second injection and disappeared in about three weeks. A most gratifying result was obtained in a case of marginal keratitis occurring in an adult (No. 49). Twenty-four hours after an intramuscular injection the redness and photophobia had disappeared, and on the third day the patient was able to read. A case of hereditary interstitial keratitis not only failed to improve after three injections, but at the end of one month the second eye became involved. The patient was finally given injections of mercury, and showed some improvement at the end of four months. Two cases of optic atrophy (Nos. 24 and 27) and one case with paralysis of the superior rectus muscle and ptosis (No. 43) showed no change as a result of treatment.

A brilliant result was obtained in the following case (No. 21): A man, aged thirty years, suddenly complained of intense hemi-crania followed by protrusion of the left eyeball downward and outward. The vision fell to mere perception of light. Examination of the fundus showed nothing abnormal. He had been infected with syphilis ten years previously, and gave a 4 + Wassermann reaction. He was given four intravenous injections, and in ten days the exophthalmos had disappeared and vision in the affected eye had improved to $\frac{20}{30}$. He had not shown any relapse at the end of five months.

The result of treatment in several cases of bone syphilis was most satisfactory. One patient (No. 47) had suffered from osteopereostitis of the tibia for two years, causing her a good many sleepless nights and some difficulty in walking. No relief had been obtained in taking mercury for a year. She was given a single intramuscular injection, after which the pain disappeared almost completely in twenty-four hours, and at the end of a month she could walk without any difficulty. Within six months she had gained fifteen pounds in weight. The improvement was also shown by the x-ray photographs, kindly taken by Dr. William H. Stewart, who reports upon them as follows: "Fig. 5, an anteroposterior view of the left tibia, shows marked productive osteitis, with here and there light shadows indicating the foci of inflammation. The picture is characteristic of the productive bone lesions of syphilis. Fig. 6, taken in approximately the same position, six and one-half months after treatment, shows a considerable change. The condensing process is not nearly as extensive, and shows general absorption. In certain places the medullary canal can be differentiated from the cortex. The areas of rarification are more extensive and cast less dense shadows, indicating further absorp-

tion. In other words, a considerable improvement has taken place."

Another patient with periostitis of the knee and ankle (No. 37) was given four intravenous injections. Although the knee had been stiff for six months, it became perfectly normal on the day after the second injection. In a case of osteoperiostitis of the femur (No. 44) of three years' duration, no improvement resulted from four intravenous injections except a lessening of pain during the night.

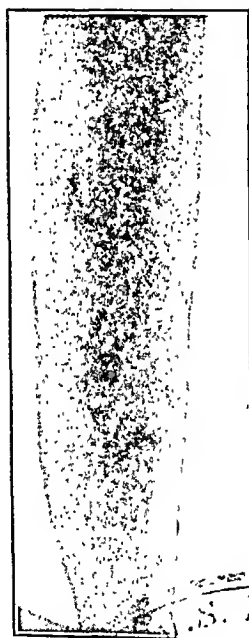


FIG. 5.—Osteoperiostitis of tibia. Before treatment.

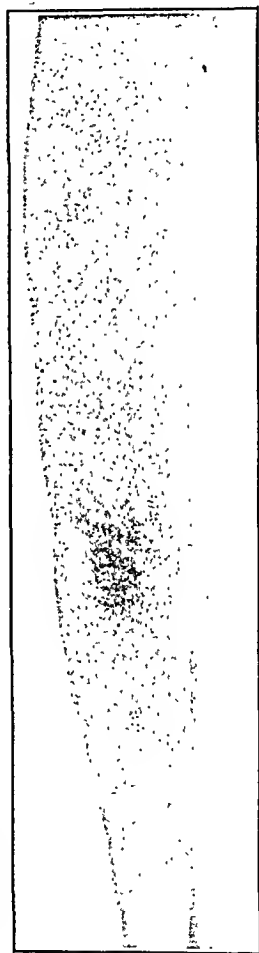


FIG. 6.—Osteoperiostitis of tibia. Six months after one intramuscular injection of neosalvarsan.

An interesting case of osteoporosis (No. 14) was treated at the request of Dr. William H. Luckett. The patient had previously suffered from four fractures of the right and three of the left femur, and at the time of treatment was recovering from another fracture of the left femur. As the Wassermann reaction was strongly positive

she was given four intravenous injections of neosalvarsan. This resulted in a lessening in the strength of the reaction, although the x -raysshowed practically no change in the bone. The condition shown in the radiograms (Figs. 7 and 8) is described by Dr. Stewart as fol-

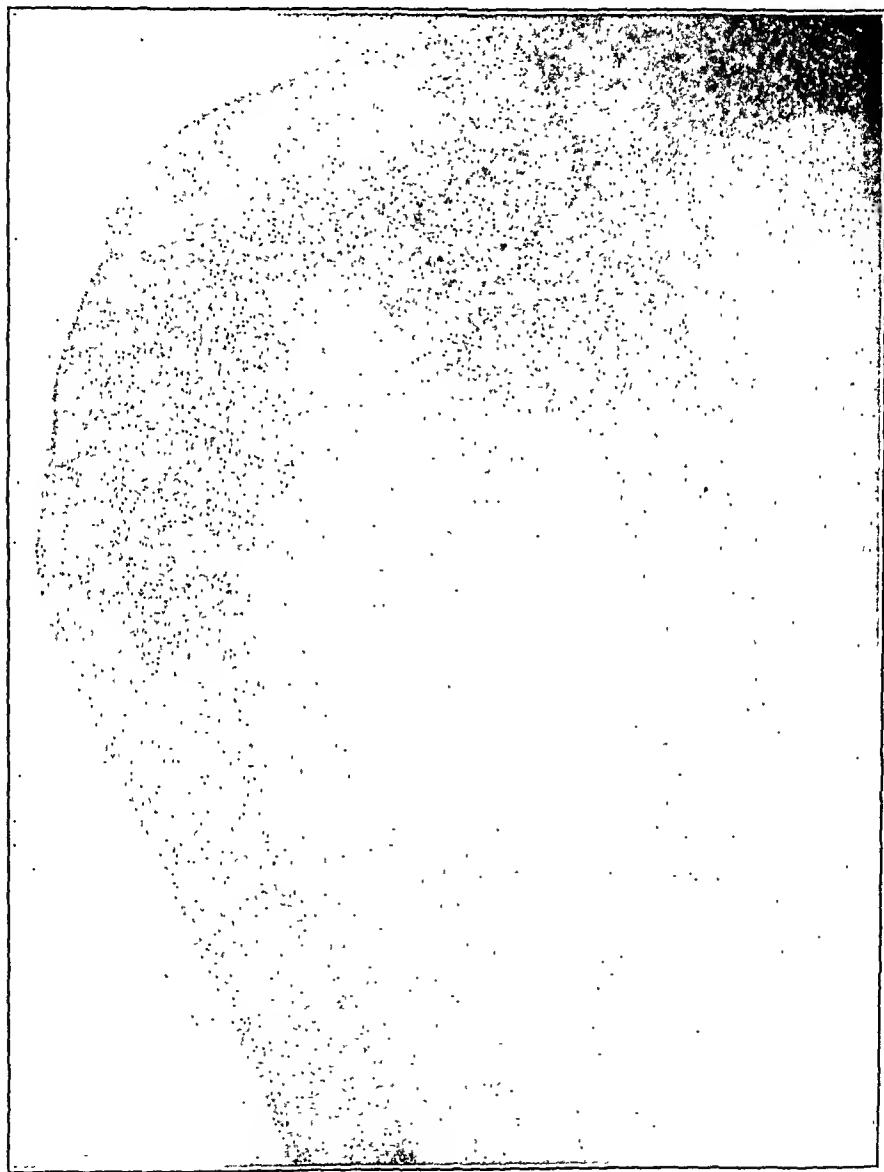


FIG. 7.—Osteoporosis.

lows: "The most typical lesions are seen in the upper third of the femur in and around the acetabulum. These portions are markedly deformed, the convex surface being directed upward, indicating the softening, the deformity being produced by the body weight.

Marked trabeculation and loss of bony substance is noticed in irregular areas. The main outline of the cortex is still retained. The condition seems to me to come under the classification of Bloodgood as cystic degeneration of bone."

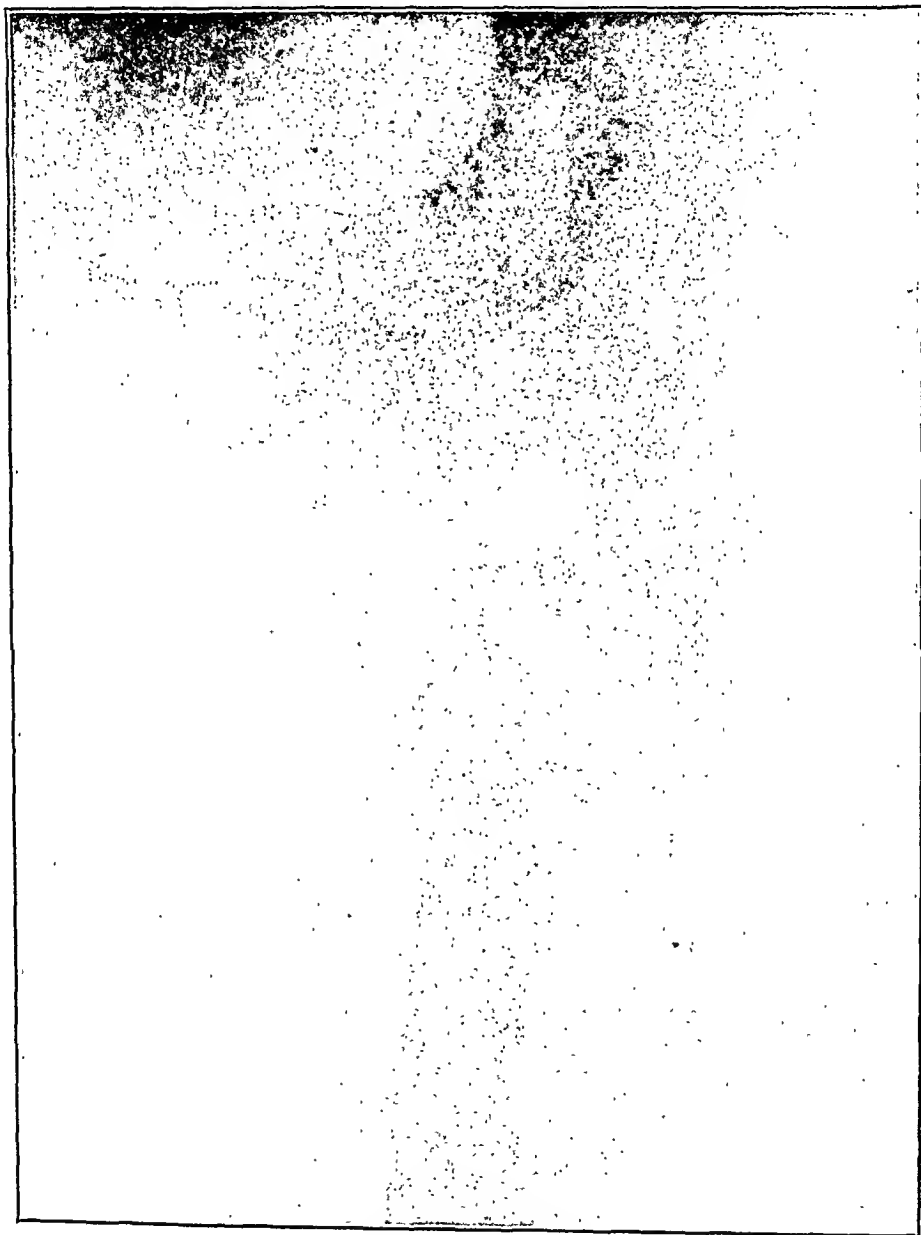


FIG. 8.—Osteoporosis.

In two cases of latent syphilis with persistent headaches there was only temporary improvement after treatment. One case of tabes (No. 4) showed an improvement in gait and in general strength, though since the last injection he has been sexually impotent.

In general the symptomatic effect of neosalvarsan was satisfactory. It was analogous to that of salvarsan, though apparently a little weaker. The effect upon the Wassermann reaction was, however, far from satisfactory, and was, in my opinion, considerably weaker than that of a corresponding amount of salvarsan. The Wassermann tests were performed so far as possible at monthly intervals. The technique that was followed was the Thomsen modification, the method employed at the Statens Seruminstitut, at Copenhagen. A definite amount of an alcoholic extract of a normal heart served as antigen, decreasing amounts of patient's serum were used, and the complement titrated.

Of 36 cases treated by three to four intravenous injections, and followed serologically on an average of over five months, 1 case became completely negative and remained so for four months; 2 became negative and 2 almost negative, but later relapsed and became partially positive. A lessening in the strength of the reaction took place in 16 cases, while in 15 cases there was no change.

In giving the intravenous injections it was unfortunately not possible to follow the request of Professor Ehrlich, to use water that was absolutely freshly distilled. A fresh supply was only obtained at intervals of two weeks. It was possibly due to this reason that in my series of 161 intravenous injections the following symptoms were noted. Chills or chilly sensations were reported after twenty-seven injections, nausea after thirty, vomiting after ten, diarrhea after three, headache after four, dizziness after six, malaise after five, and abdominal cramps after three injections. Many of these symptoms were extremely mild, and did not prevent the patients from returning for further injections, which were given with fairly great regularity, as can be seen by a glance at the accompanying tables. In a single case (No. 38) the patient felt sick enough to be taken into the hospital for three days. He complained of severe nausea, general pains, and presented an edema of the face. The temperature, however, did not rise above 100°.

Among the general effects of the treatment with neosalvarsan should be mentioned an improvement in appetite, which occurred in a great majority of cases. A gain in weight was also frequently observed, 11 patients gaining an average of thirteen pounds while 1 woman gained twenty-six pounds in six months.

There was no disturbance in the menstrual function in any case.

The Herxheimer reaction was particularly marked in 2 cases (Nos. 32 and 36), being noted by the patients themselves. In another case (No. 31) an erythematous rash appeared upon the face, arms, and legs four days after injection lasting two days,

and being accompanied by a temperature of 100° and slight malaise:

The local effects of the intravenous injections were much less disturbing to the veins than injections of salvarsan. They varied from the formation of a tiny nodule to complete occlusion of the vein. The disturbance was so slight, as a rule, that four injections could frequently be given in the same vein within a period of nine days, which would seldom be possible in the case of salvarsan.

The technique of preparing the new remedy with water at room temperature, dispensing with the alkali, etc., is too well known to be discussed in this report. It is sufficient to say that in no case was the vein exposed by cutting down upon it. This procedure, in my opinion, should be avoided whenever possible, as it not only leaves a compromising scar, but destroys any further usefulness of the vein for injection or blood-letting purposes. By inserting the needle directly through the skin much time is also saved. In this way it was possible to give five injections in an hour, with a skilled nurse as an assistant.

The intramuscular method was tried in 11 cases, the remedy being given as an emulsion with iodopin oil. It must be admitted that the results in some of these cases were exceedingly good, and compared favorably with those obtained by repeated intravenous injections. They were, however, decidedly painful in all except two of the cases. The pain, induration, and lameness that followed more than counterbalanced the time and trouble of giving several injections by the intravenous method. Though the experience quoted in this report is limited, I think it is fair to draw the following conclusions:

CONCLUSIONS. 1. Neosalvarsan is an excellent symptomatic remedy for the treatment of syphilis.

2. Its symptomatic action seems to be slightly weaker than salvarsan when used in corresponding amounts.

3. Its serological action seems to be considerably weaker than salvarsan when used in corresponding amounts.

4. It possesses a decided advantage over salvarsan in the greater ease and rapidity with which it can be prepared and injected intravenously.

5. Intravenous injections of neosalvarsan are much less disturbing to the veins than intravenous injections of salvarsan.

For the greater part of the material in this report I am indebted to Drs. Edward Pisko, Benjamin F. Ochs, and Wilmot B. Allen, to whom I wish to express my thanks.

TABLE I.—Cases of Syphilis Treated with Intravenous Injections of Neosalvarsan.

No.	Sex.	Age.	Stage of disease.	Duration of lesions.	Previous treatment.	Neosalvarsan injections.	Clinical results.	Wassermann reaction.
1	F.	40	Papular syphilide	6 weeks	None	Gm. 0.5, June 12 Gm. 0.5, June 14 Gm. 0.5, June 17	Eruption disappeared 3 days after last injection.	Changed from 4 + to 3 + at end of 6 months. 4 + at end of 9 months.
2	F.	27	Papular syphilide	6 weeks	Hg, internally 10 days	Gm. 0.5, June 19 Gm. 0.4, June 14 Gm. 0.4, June 17 Gm. 0.4, June 19 Gm. 0.4, June 21	Eruption disappeared 2 weeks after last injection.	Remained 4 + at end of 9 months.
3	M.	60	Gumma of leg	1 month	None	Gm. 0.4, June 21 Gm. 0.6, June 14 Gm. 0.6, June 17 Gm. 0.6, June 19 Gm. 0.6, June 21	Gumma healed in 3 months.	Changed from 4 + to 2 + at end of 5 months. 4 + at end of 9 months.
4	M.	53	Tubes	Infection 20 years previously	None	Gm. 0.6, June 19 Gm. 0.6, June 21 Gm. 0.6, June 23 Gm. 0.6, June 29	Improvement in gait and general strength. Impotent since treatment.	Changed from 3 + to negative at end of 3 months. 3 + at end of 9 months.
5	F.	19	Papular syphilide	3 weeks	None	Gm. 0.3, July 1 Gm. 0.3, July 3 Gm. 0.3, July 5 Gm. 0.3, July 8	Eruption disappeared 2 weeks after last injection.	Changed from 4 + to negative at end of 2 months. 2 + at end of 8 months.
6	M.	20	Papulopustular syphilide	2 weeks	None	Gm. 0.3, July 1 Gm. 0.4, July 3 Gm. 0.4, July 5 Gm. 0.4, July 8	Pustules dried after 3d injection. Crusts fell 2d day after 4th injection.	Changed from 4 + to 3 + at end of 2 months. Remained same at end of 7½ months.
7	M.	28	Gumma of the uvula	1 month	None	Gm. 0.4, July 1 Gm. 0.4, July 3 Gm. 0.4, July 5 Gm. 0.4, July 8	Gumma healed 24 hours after 3d injection.	Changed from 4 + to 3 + at end of 2 months. Remained same at end of 7½ months.
8	M.	30	Maculopapular syphilide	2 weeks	None	Gm. 0.4, July 15 Gm. 0.3, July 17 Gm. 0.4, July 17 Gm. 0.5, July 22 Gm. 0.5, July 24	Failed to return to clinic. Later went to Central Islip Hospital where he is said to have shown symptoms of cerebral syphilis.	Wassermann performed at Islip said to have been negative.
9	F.	24	Papular syphilide	3 weeks	None	Gm. 0.3, July 15 Gm. 0.4, July 17 Gm. 0.5, July 21 Gm. 0.6, July 24 Gm. 0.6, July 26	Eruption disappeared 1 month after last injection. Patient gained 26 pounds.	Changed from 4 + to 1 + at end of 3½ months. Remained same at end of 7½ months.
10	M.	33	Superficial ulcers of tongue. Pains in tibiae	3 years of disappearing and recurring	Hg, irregularly in small doses	Gm. 0.3, July 17 Gm. 0.3, July 17 Gm. 0.4, July 17 Gm. 0.4, July 17 Gm. 0.5, July 22	Ulcers healed 24 hours after 2d injection. Pains in tibiae disappeared same time. No recurrence at end of 8 months.	Changed from 3 + to 2 + at end of 7½ months.

11	F.	40	Nodular syphilide of neck. Gumma of leg	Nodular syphilide 15 months. Gumma 1 year	None	Gm. 0.3, July 17 Gm. 0.4, July 24 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Lesion upon neck healed 3 days after 3d injection. Gumma of leg not entirely healed at end of 8 months. Eruption disappeared 4 days after last injection.	Changed from 4 + to 3 + at end of 2 months. 2 + at end of 8 months.
12	M.	39	Nodulosquamous syphilide of arms, shoulders, and back	9 years	None	Gm. 0.3, July 24 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption nearly gone at time of last injection. Failed to return to clinic.	Changed from 4 + to 2 + at end of 6 weeks. 2 + at end of 7 months.
13	M.	23	Pustular syphilide	2 months	Hg. internally 4 months	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption nearly gone at time of last injection. Failed to return to clinic.	Changed from 4 + to 2 + at end of 6 weeks. 2 + at end of 7 months.
14	F.	39	Osteoporosis. Fracture of femur	None	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption nearly gone at time of last injection. Failed to return to clinic.	Changed from 4 + to 2 + at end of 6 weeks. 2 + at end of 7 months.
15	F.	30	Gumma of leg	1 month	No Hg.; 1 intra-venous salvarsan 1 year previously.	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption disappeared 1 month. (See text for eye complications.)	Remained 4 + at end of 6 months.
16	F.	27	Annular papular syphilide	3 months	None	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption disappeared 1 month. (See text for eye complications.)	Remained 4 + at end of 6 months.
17	M.	49	Nodular syphilide of penis; leukoplakia; ulcers of mouth	Nodular syphilide and ulcers 6 weeks	Hg. internally for 6 months	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Nodular lesions disappeared in 1 week, and ulcer 2 days after last injection. No objective change in leukoplakia.	4 + at end of 5½ months.
18	M.	40	Maculopapular syphilide	4 months	Hg. internally for 1 month	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption disappeared 10 days after last injection.	Changed from 4 + to 3 + at end of 8 weeks. 2 + at end of 5½ months.
19	M.	44	Macular syphilide	1 month	None	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Eruption disappeared 6 days after last injection. Failed to return to clinic.	Changed from 4 + to 3 + at end of 8 weeks. 2 + at end of 5½ months.
20	M.	22	Gumma of fauces	1 month	Hg. internally for 2 weeks	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Gumma healed 3 days after 4 + at end of 6 weeks, 2d injection.	Changed from 4 + to 3 + at end of 6 weeks. 2 + at end of 5½ months.
21	M.	30	Exophthalmos	2 weeks	None	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Exophthalmos disappeared in 2 weeks. (See text.)	4 + at end of 3 months. 3 + at end of 5 months.
22	F.	26	Pustular syphilide	1 month	None	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Pustules dried 1 week after first injection.	Changed from 4 + to 2 + at end of 4 months. 4 + at end of 5½ months.
23	M.	26	Latent syphilis. Persistent headaches	1 injection of salvarsan 2 years previously	Gm. 0.3, July 24 Gm. 0.4, July 29 Gm. 0.5, July 29 Gm. 0.6, July 29 Gm. 0.3, July 29 Gm. 0.4, Aug. 2 Gm. 0.5, Aug. 6 Gm. 0.6, Aug. 8 Gm. 0.3, July 29 Gm. 0.4, July 30 Gm. 0.5, Aug. 2 Gm. 0.6, Aug. 5 Gm. 0.3, Sept. 7 Gm. 0.4, Sept. 9 Gm. 0.5, Sept. 11 Gm. 0.6, Sept. 13 Gm. 0.3, Sept. 11 Gm. 0.4, Sept. 13 Gm. 0.5, Sept. 16 Gm. 0.3, Sept. 16 Gm. 0.4, Sept. 18 Gm. 0.5, Sept. 20 Gm. 0.6, Sept. 22 Gm. 0.3, Sept. 23 Gm. 0.4, Sept. 25 Gm. 0.5, Sept. 27 Gm. 0.6, Sept. 30	Headaches disappeared for 2 months and then returned.	Remained + at end of 3 months.

No.	Sex.	Age.	Stage of disease.	Duration of lesions.	Previous treatment.	Neosalvarsan injections.	Clinical results.	Wassermann reaction.
24	F.	32	Chorioretinitis. Optic atrophy	Vision began to fail 5 months previously	5 Hg. injections	Gm. 0.4, Oct. 14 Gm. 0.5, Oct. 16 Gm. 0.6, Oct. 18 Gm. 0.3, Oct. 16 Gm. 0.4, Oct. 21 Gm. 0.5, Oct. 23 Gm. 0.4, Oct. 18 Gm. 0.5, Oct. 21 Gm. 0.6, Oct. 23 Gm. 0.4, Oct. 21 Gm. 0.5, Oct. 25 Gm. 0.6, Oct. 23	No improvement. Slight improvement. No change.	Remained 2 + at end of 7 weeks. 1 + at end of 6 months. 3 + at end of 7 weeks. Same at end of 6 months. Changed from 4 + to 1 + at end of 5 weeks. Changed from 4 + to 3 + at end of 5 weeks. 2 + at end of 5 months. Remained 4 + at end of 5 months.
25	M.	17	Latent	6 months after infection	None			
26	F.	20	Latent syphilis Severe headaches	Headaches 18 months	None			
27	M.	49	Optic atrophy	1 year	None			
28	F.	14	Hereditary syphilis Interstitial keratitis	1 month	None	Gm. 0.4, Oct. 21 Gm. 0.5, Oct. 23 Gm. 0.6, Oct. 23	Slight improvement at end of 1 month, when other eye became involved. Both eyes improved at end of 4 months. Lesions disappeared 2 days after 2d injection. 	
29	F.	27	Mucous patches of vulva	2 months	None	Gm. 0.4, Oct. 21 Gm. 0.5, Oct. 23 Gm. 0.6, Oct. 25 Gm. 0.4, Oct. 23 Gm. 0.5, Oct. 30 Gm. 0.6, Nov. 1 Gm. 0.4, Nov. 4 Gm. 0.5, Nov. 6 Gm. 0.6, Nov. 8	Changed from 4 + to 3 + at end of 5 weeks. Remained same at end of 5 months. Remained 3 + at end of 5½ months.	
30	M.	28	Latent syphilis	3 years after infection	Hg. internally for 2½ years irregularly			
31	F.	24	Maculopapular syphilitide; condylomata	2 months	None		Eruption disappeared 2½ weeks after last injection. Condylomata disappeared in 5 weeks.	Changed from 4 + to 1 + at end of 8 weeks. Remained 1 + at end of 4½ months.
32	F.	33	Maculopapular syphilitide; iritis	3 weeks	None	Gm. 0.4, Nov. 4 Gm. 0.5, Nov. 6 Gm. 0.6, Nov. 8	Iritis cleared up in 3 weeks. Eruption still present, though fading, at end of 2 months.	4 + at end of 9 weeks.
33	M.	22	Annular papular syphilitide	5 weeks	None	Gm. 0.4, Nov. 6 Gm. 0.5, Nov. 8 Gm. 0.6, Nov. 11 Gm. 0.5, Nov. 13 Gm. 0.4, Nov. 11 Gm. 0.5, Nov. 13 Gm. 0.6, Nov. 15	Lesions flattened completely in 2½ hours after 2d injection. Pigmentation remaining.	
34	M.	21	Mucous patches; pigmentary syphilide	4 months	Hg. internally for 1½ weeks		Mucous patches healed 48 hours after 1st injection. Pigmentary syphilide partially disappeared at end of 4 months.	Changed from 3 + to 2 + at end of 5 weeks. 1 + at end of 2 months. Negative at end of 4 months.

35	F.	21	Iridocyclitis	2 months	None	Gm. 0.5, Nov. 18 Gm. 0.6, Nov. 20 Gm. 0.6, Nov. 27	Iridocyclitis cleared up in 3 weeks.	Remained 3 + at end of 2 months.
36	F.	30	Macular syphilide	4 weeks	Hg. internally for 2 weeks	Gm. 0.6, Nov. 29 Gm. 0.4, Nov. 18 Gm. 0.5, Nov. 20 Gm. 0.6, Nov. 25 Gm. 0.6, Nov. 27	Eruption disappeared 1 week after 2d injection; 2 months later, sparse eruption of lenticular papules.	Remained 4 + at end of 4 months.
37	M.	26	Osteoperiostitis of knee and ankle	6 months	Hg. internally for 2 months	Gm. 0.3, Nov. 27 Gm. 0.4, Nov. 29 Gm. 0.5, Dec. 2 Gm. 0.6, Dec. 6	Knee, which had been stiff and painful for 6 months, became practically normal after 2d injection. (See text.)	
38	M.	25	Periosteal gumma	6 weeks	Hg. internally for 6 months	Gm. 0.3, Nov. 27 Gm. 0.5, Nov. 29 Gm. 0.6, Dec. 2	Gumma disappeared 10 days after last injection.	Remained 4 + at end of 4 months.
39	M.	22	Gumma of tongue	1 month	Hg. internally for 3 years	Gm. 0.5, Nov. 27 Gm. 0.6, Dec. 4 Gm. 0.6, Dec. 6 Gm. 0.6, Dec. 11	Gumma completely healed 7 weeks after last injection.	Changed from 4 + to 3 + at end of 10 weeks.
40	M.	43	Nodular syphilide of scalp. Gumma of arm	Nodular syphilide for 3 months; gumma, 1 month	Hg. internally, and by inunctions small amounts	Gm. 0.3, Dec. 6 Gm. 0.4, Dec. 9 Gm. 0.5, Dec. 11 Gm. 0.6, Dec. 11	Lesions healed 3 weeks after last injection.	Remained 4 + at end of 3 months.
41	F.	25	Mucous patches of vulva and mouth	2 weeks	None	Gm. 0.3, Dec. 4 Gm. 0.4, Dec. 6 Gm. 0.5, Dec. 9	Lesions healed at time of 3d injection; failed to return to clinic.	
42	M.	26	Ulcerating nodular syphilide	None	Gm. 0.3, Dec. 13 Gm. 0.4, Dec. 16 Gm. 0.5, Dec. 18 Gm. 0.6, Dec. 20	Failed to return to clinic.	
43	F.	52	Paralysis of superior rectus; ptosis	6 months	Hg. internally for 5 months	Gm. 0.4, Dec. 18 Gm. 0.5, Dec. 20	No improvement.	Remained 4 + at end of 3 months.
44	M.	59	Osteoperiostitis	3 years	Hg. internally for 3 years irregularly	Gm. 0.3, Dec. 30 Gm. 0.4, Jan. 3 Gm. 0.5, Jan. 6 Gm. 0.6, Jan. 8	Pain lessened; no change in size of leg. (See text.)	Remained 2 + at end of 10 weeks.
45	M.	40	Gumma of back	3 weeks	None	Gm. 0.5, Jan. 10 Gm. 0.5, Jan. 13	Lesions healed 4 weeks after last injection.	Remained 4 + at end of 3 months.

TABLE II.—Cases of Syphilis Treated with Intramuscular Injections of Neosalvarsan.

No.	Sex.	Age.	Stage of disease.	Duration of lesions.	Previous treatment.	Neosalvarsan injections.	Clinical results.	Wassermann reaction.
46	F.	42	Pustular (cupial) syphilide	6 weeks	Hg. internally for 6 weeks	Gm. 0.4, June 12	Lesions healed in 9 weeks.	2 + at end of 3 months.
47	F.	38	Osteoperiostitis of tibia	2 years	Hg. internally for 1 year	Gm. 0.4, June 23 Gm. 0.6, Sept. 21	Pain disappeared at end of 24 hours.	Remained same at end of 9 months. Remained 3 + at end of 6 months.
48	F.	37	Latent syphilis; carcinoma of uterus	None	Gm. 0.3, Nov. 6		
49	F.	38	Marginal keratitis	1 week	None	Gm. 0.6, Nov. 8	Redness and photophobia disappeared on 2d day. (See text.)	Changed from 4 + to 2 + at end of 8 weeks.
50	F.	28	Moist papules	2 months	None	Gm. 0.6, Dec. 2	Lesions healed in 3 days.	Remained same at end of 4½ months.
51	F.	24	Gummas of legs and eyelid	On legs 1 month; on eyelid 3 months	Hg. internally for 9 months	Gm. 0.6, Dec. 2	Ulcers of legs partially healed end 3 months; gumma of eyelid well in 1 month.	3 + at end of 5 weeks.
52	F.	38	Gumma of nasal septum	1 month	None	Gm. 0.6, Dec. 2	Gumma nearly healed 4 days after last injection.	
53	F.	49	Periosteal gumma of forehead	5 months	None	Gm. 0.6, Dec. 9	Left clinic and was treated at Mt. Sinai Hospital by 7 injections of neosalvarsan; gumma not completely healed at end of 3 months.	
54	F.	36	Exophthalmos; severe headaches	3 months	None	Gm. 0.6, Dec. 9	Failed to return to clinic.	
55	F.	24	Ulceration of cervix	10 days	2Hg. injections	Gm. 0.6, Dec. 30	Ulceration healed in 2 weeks.	Remained 4 + at end of 10 weeks.
56	F.	38	Ulcerating gumma of leg	18 months	Hg. internally for 18 months	Gm. 0.6, Jan. 3	Ulcers healed at end of 1 month.	Remained 4 + at end of 10 weeks.

THE METABOLISM, PREVENTION, AND SUCCESSFUL TREATMENT OF RHEUMATOID ARTHRITIS: SECOND CONTRIBUTION.¹

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(Continued from December, 1913.)

CASE VII.—Mrs. E., aged forty-seven years, white. Referred by Dr. James E. Talley. This case was of great interest, and was made the subject of a metabolic study. The patient had led an active, useful life in a country village, and considered herself healthy. She had had no children and no miscarriages. Six years previous to admission her ovaries had been removed at the German Hospital, Philadelphia, for pelvic trouble, but she apparently made an uneventful recovery. Shortly after this, however, she experienced at times, in several fingers, a blanching and numbness which were aggravated or precipitated by cold weather. Immersion in hot water restored normal sensation, and, as this appeared, the color changed from white to red and finally purple before the normal hue returned.¹ After persisting a year or so the condition cleared up, except for a very rare and slight suggestion of it in very cold weather.

For a few years past she had been subject to some "sore throat" during the winter months, and had been troubled with belching and headache. Her bowels had always been costive. In the latter part of June, 1912, her left knee became swollen and stiff, followed in two weeks by the right. Since then her ankles, wrists, hands, shoulders, and hips had become involved, until on September 11, on admission to the Presbyterian Hospital, Philadelphia, she could walk only with assistance, and said that for six weeks previously she had been forced to sit all of the time without much changing her position. Appetite was good, but sleep was much disturbed by pain. Examination showed good development and nutrition, with a freely movable right kidney. The wrists, fingers, knees, and ankles were all swollen and somewhat tender upon motion, but, presented no other marked deformity. Examination of the ears and nasopharynx, by Dr. Ben. C. Gile, revealed no focus of infection. The teeth were well cared for. The urine was essentially normal, and was free from indican. Blood examination showed: Red-blood cells, 3,640,000; white-blood cells, 10,400; hemoglobin, 59 per cent. X-ray examination of the abdomen showed marked dilatation

¹ Dr. C. B. Farr kindly furnished me with this information from observations made when the patient was under his care. He regarded the condition as suggestive of Raynaud's disease, which has been mentioned by some writers as occasionally prodromal to rheumatoid arthritis.

and ptosis of both stomach and colon, with great elongation and tortuosity of the bowel. The hands and other joints showed both hypertrophic and atrophic changes. Under large doses of salicylates her symptoms improved, and she was advised to leave the hospital, take Fowler's solution, and report for frequent observation until her anemia had improved sufficiently to warrant treatment along the lines to be mentioned presently.

Experience with Case II had seemed to indicate this course, but subsequent study showed it to have been needless. She was treated with arsenic, tonics, ample feeding, and good hygiene, however, from October 23 to December 15, with improvement in her general health and anemia, and subjective improvement in her joints, though swelling and stiffness and pain still persisted.

December 15 she was readmitted to the hospital. At this time she had daily fever up to about 100° or more, a blood pressure of 124 and 60, and weighed $121\frac{1}{4}$ pounds. For three weeks previously, through a misunderstanding in regard to getting a private room, she had had no arsenic, and was consequently in much pain and discomfort, having pain at night, and being greatly limited in all her movements.

This was deemed a good case in which to study the metabolism, and she was accordingly placed upon the following diet, with the idea of making the observations while she was in an active stage of the disease for the purpose of contrasting them with others made in convalescence.

December 27. She ingested in twenty-four hours the following, divided into three meals: Sugar, 12 grams; butter, 30 grams; toast, 55 grams; egg, 100 grams; rice, 210 grams; milk, 690 c.c.; salt, $1\frac{1}{2}$ grams. This approximated 1375 calories, which with her weight, about 119 pounds gave 11.5 calories per pound of body weight or 25.30 calories per kilo. She had been placed previously for several days upon an unrestricted diet of the above ingredients, with the idea of determining how much of this food she needed and would take during the "metabolic" period. The above figures were therefore of her own choosing. The metabolic figures follow later in the text and are there discussed.

January 1, 1913. Upon the completion of these observations she was placed under the following regimen:

Colonic lavage once a day in the morning; 7 glasses of whole milk daily; 1 slice of toast and butter at breakfast; 1 apple at breakfast; 1 green vegetable at lunch (either spinach, lettuce, celery, turnips, cabbage, or tomatoes), provided it be not cooked with sugar or flour; 1 slice of toast and butter at supper; 1 helping of stewed fruit at supper. This yielded about 1434 calories, slightly more than the first diet, but the calories were differently distributed. In the first period, of the 1375 calories about 200 had come from proteid, about 620 from fat, and about 540 from carbo-

hydrates. In the second diet of about 1434 calories, about 220 had come from proteid, about 753 from fat, and about 461 from carbohydrates. These figures show that the carbohydrates gave fewer and the fats gave more of the total calories in the second than in the first period. This will be referred to later.

The notes made at the time as to her condition here follow under their respective dates:

December 19, 1912. Patient was getting worse steadily; hands were enlarged and knees were painful. Slept fairly well. Appetite was good. Was getting house diet. Had been without arsenic for nearly a month, owing to difficulty of getting a room. For ten days after the drug was stopped she still felt its benefit.

December 28. Metabolic diet began December 24. Bowels well moved at that time, but only slightly since by salt solution or enema. This date distilled water instead of salt solution was used. Had been increasingly poorly since admission until this date. At 5 P.M. said she felt better than she had for two weeks, and could arise from her chair and move her fingers well. Seemed to be losing weight; tongue clean; expression bright.

December 29. Said she felt "pretty good." Not quite so free from stiffness, etc., as the day before, but the difference was not great, and she ascribed it to the constipation. Slept well the previous night. Last three nights had been good. No stool as yet; nothing but scybalous masses the size of a peanut. Tongue clean.

December 30. Knees were slightly stiff to-day, and shoulders also, more so than on previous day. Could move fingers more than five days before. They could be shut passively almost entirely, and there was less swelling. A ring which was tight on admission could be moved to the knuckle freely, and moved around finger. Had less soreness at the left trochanter than prior to December 27. Bowels moved well after enema yesterday at 3 P.M. Patient said she felt a good deal better than one week before; generally, as well as in joints.

December 31. Was slightly worse. Weight now constant at 118½ pounds. Had more pain at night and fingers were more swollen, the right hand being worse than the left. Temperature was apparently working down slightly.

January 1, 1913. Therapeutic diet started.

January 3. Had been on the therapeutic modified diet, seven glasses of milk, etc., since January 1. Slightly better yesterday and slightly improved this date also. Hands not swollen, though all the joints were stiff on waking.

January 4. Unquestionably better. Had a good night, with no severe pain, and slept well. Walked better. Hands were not swollen and fingers hurt only on marked flexion, active or passive. Temperature was lower than for any extended period yet.

January 6. Right knee and right ankle were not quite so well as the day before. Everywhere else she was better. Hands were smaller; could be bent farther and with less stiffness and pain; motions were distinctly quicker than before. Could move both shoulders better, and had a good night. Temperature was barely above 99°. Weight was the same.

January 8. Could not use hands quite so well, though she could hold her hands closed when they were shut. Had slightly more stiffness in the shoulders, as tested by putting her arm over the back of a chair when sitting. Had slightly more pain in her knees, though she could arise fairly well. Temperature seemed to be working lower; hands looked distinctly smaller; the metacarpals showed plainly. Said she felt pretty well, and that bad weather always made her feel worse. Said she would willingly continue on her present diet, even, to retain the improvement to date, such as it was.

January 11. Hands closed better than at any time. Knees were slightly stiffer. Left shoulder pained slightly during the night, but could be moved freely and without pain. No fever. Weight constant. Could pick up heavy books with her hands. Not too hungry, but enjoyed her food. Left hand could be shut passively, and forcibly held without pain.

January 29. Slight "lameness" in both shoulders, especially the left. Motion not so free as previously at one time. "Hands are fine." Insists that she had not felt so well for a long time. Temperature was normal.

February 6. Had stiffness and pain at the angle of the jaws on both sides since onset of disease. Had noticed in this respect an improvement for three to four days previously; this date it was distinctly marked.

February 8. Walked five squares the previous day. Knees were no worse. Shoulder was better. Middle finger of right hand was swollen and sore; began the day before at 4 P.M. Better than during the night. Used finger with a thimble and pressed quite hard while sewing.

February 9. Walked seven squares the day before. Finger was much better. Shoulder also was much better than for two weeks past. Knees were pretty fair.

March 9. Walked the previous day better than at any time yet. Climbed three flights of stairs in the afternoon. Feet and ankles hurt slightly during the night.

March 12. Had been taking an egg at each meal, beginning the day before at lunch. No rise of temperature, and felt well. Slept well at night. Very supple. Was given more cream in coffee today.

March 15. Going home. Bad, rainy day, but felt very well.

At the time of leaving the hospital her weight was 117. Her dietary was as follows:

6.30 A.M.: Milk, 200 c.c.

Breakfast: 1 apple, 150 grams; weak coffee, 120 c.c., with $\frac{1}{3}$ of 20 per cent. cream and $\frac{1}{3}$ of sugar; 1 soft-cooked egg; toast, 16 grams (one-half slice); butter, 13 grams.

10.30 A.M.: Milk, 200 c.c.

Dinner: Bouillon, 120 c.c.; 4 tablespoonfuls of stewed tomatoes; 1 soft-cooked egg; toast, 15 grams; butter, 13 grams; lettuce with 1 tablespoonful of mayonnaise dressing; milk, 1 glass, 200 c.c.

3.30 P.M.: Milk, 200 c.c.

Supper: 1 soft-cooked egg; toast, 15 grams; butter, 13 grams; baked apple, 158 grams; 3 stalks of celery; milk, 1 glass, 200 c.c.

Upon reaching her home the colonie lavage was given every other day for a week and then discontinued entirely. Little by little substitutions and additions were made to her dietary, bearing in mind the caloric values of the foods given, and an effort was made to increase her weight with additions of cream to her milk.

This was successful, so that by May 15, she was able to do a large part of her housework, and weighed 122½ pounds, notwithstanding her greatly increased activities and responsibilities.

She was emphatic in stating that her general health was better than it had been before she was taken ill, that she was free from the gastric distress and headache, which had been frequently present, and that her only complaint was slight stiffness in the evening after reading for an hour or so in one position. Her sleep was excellent, unbroken by any pain, and her spirits were bright.

May 24. Her dietary averaged as follows:

Breakfast: 1 apple; 1 slice of toast and butter; 1 soft-boiled egg; 1 cup of hot water with 1 teaspoonful of cream and 1 teaspoonful of sugar.

10.30 A.M.: 1 glass of milk, with 1 tablespoonful of cream.

Dinner: 1 slice of toast and butter; 1 piece of chicken; 1 tablespoonful of beets; 2 tablespoonful of peas; 1 glass of milk and 1 tablespoonful of cream.

3.30 P.M.: 1 glass of milk, with 1 tablespoonful of cream.

Supper: 1 slice of toast and butter; 1 scrambled egg; lettuce, with French dressing; 2 tablespoonfuls of stewed rhubarb; 1 glass of milk, with 1 tablespoonful of cream.

8.30 P.M.: 1 glass of milk, with 1 tablespoonful cream.

The patient had been constant and careful in adherence to her regimen. She wanted no more than she was taking, and craved no other food, though her appetite was good. June 2, 1913, she weighed 125½ pounds, 4 pounds more than on admission to the hospital, when she had been taking arsenic, tonics, and forced feeding, and over 8 pounds more than she weighed at one time during the early stages of her therapeutic diet.

About June 27, in the midst of a protracted spell of hot weather, this patient had a regrettable but interesting relapse. She did not appear for treatment until the relapse had lasted ten days, though she had made some reductions of her diet of her own accord. When seen her fingers and wrists were swollen and she complained of her hips. Her diet was further reduced and she was put at rest. On July 1 she was distinctly better, though still not well. In November, 1913, her joints were in fairly good condition and she was adhering to the principles of her diet, but the symptoms of Reynaud's disease had become more constant and considerably more advanced.

This and certain other observations of a similar nature seemed to indicate that during hot weather, when the bodily calorie need is much reduced, the particular calorie intake which has been well tolerated or has been a necessity may become a surfeit, with the result just described. During protracted heat the calorie necessity and tolerance probably decrease, and in the presence of an unstable metabolic equilibrium the adjustment might easily be overthrown.

It should be noticed that this patient had been living presumably near her high limit of food tolerance before this relapse, as she had gained markedly in weight and had been eating relatively freely. An additional complicating factor in this case is the vasomotor instability, as evidenced by her previous attacks suggesting Raynaud's disease. For several weeks before the relapse above described she had had curious areas of local erythema on the palms of her hands or fingers, accompanied often by great itching. The full significance of this accompanying complication cannot be known, but there is little doubt that it aggravated her condition.

CASE VIII.—B. de H., female, white, aged thirty-two years. Referred by Dr. William Drayton, Jr., from the dispensary service of the Orthopædic Hospital. As the patient had suffered from the condition for eighteen years and presented much deformity, treatment was undertaken largely with the idea of testing the limitations of the therapeutic methods employed. The patient gave a history of having had tonsillitis nearly every winter from six to eighteen years of age, though no operation had ever been performed. Her general health had been good, however. Her present trouble began eighteen years ago in the right knee, where she noted a grating and cracking upon flexion. Within a few years her fingers, wrists, arms, and shoulders became involved, and she said that the pain was exquisite.

The disease progressed steadily, although she was treated for two years at the dispensary of the University of Pennsylvania, and had neglected no opportunity to obtain relief. She also was attended for six years or more as a private patient by the same physician who attended her at the dispensary. Two years ago she began treatment at the dispensary of the Orthopædic Hospital,

where she obtained some benefit from baking and Swedish movements, though the course of the disease was apparently not influenced. Through breaking up and stretching the adhesions, etc., she acquired some increase of motion, and her general health was benefited by tonic treatment.

During the two years of attendance at the Orthopædic Hospital Dispensary some days were spent in the ward for closer study.

Examination showed a rather stout and well-developed woman of good color and intelligence. Frequent examination of the ears, nose, throat, and teeth revealed no focus of infection, and the teeth were well cared for. A fruitless search had been conducted for many years on the above basis of infection.

The right shoulder was slightly larger than the left and the bones felt thickened. Passive motion gave distinct crepitus on both sides, and she could not raise her right arm to comb her hair. The elbows showed thickening, crepitus, and limitation of motion. The right knee was enlarged and held flexed to 60 degrees, and the tendons were rigid. Crepitus was marked, and voluntary motion was limited to about two inches.

The arches of the feet were flat, the ankles were thickened, and crepitus was readily felt in them also. There was marked enlargement of the bone ends in the hands and wrists. The fingers were mostly hyperextended and deviated to the ulnar side, though there was also marked flexion and apparent ankylosis in some. In short, the condition was typical of advanced rheumatoid arthritis. The urine was essentially normal. Blood examination showed red-blood cells, 3,550,000; white-blood cells, 9600; hemoglobin, 58 per cent. The blood-pressure was 120 systolic and 80 diastolic, and the body weight 141 pounds.

An x-ray examination by Dr. Newcomet showed the colon to be greatly elongated, and sharply bent upon itself at the hepatic and splenic flexures. The stomach was dilated and ptosed, and was divided into an upper and lower pole by the impingement of the bowel. The hands showed marked hypertrophic and atrophic changes (Fig. 1).

On admission she was allowed to eat whatever and as much as she chose of the house diet, and a record was kept of this in terms of table and teaspoons, glassfuls, etc., and when necessary some articles were weighed. A rather close approximation could thus be made of the caloric value of her food by consulting suitable tables.² The itemized figures for the respective meals during this period have unfortunately been mislaid, but the sum totals for an average twenty-four hour period are given below: Bread, 6 slices; milk, 3 glasses; egg, 1 glass; oatmeal, 2 tablespoonfuls; sugar, 1 dessertspoonful; potatoes, 2 tablespoonfuls; chicken, 50

² Food Values, by Edwin A. Locke, 1911.

grams; spinach, 2 tablespoonfuls; custard, 2 tablespoonfuls. Total about 1662 calories, though she sometimes ate more. Weight, 137 pounds, about. Calories per 1 pound body weight, about 12 or 26 per kilo. While upon this diet, about ten days, she was in much discomfort.



FIG. 1.—Case VIII. Type of elongated and tortuous colon described. The reproduction imperfectly illustrates the condition.

Observations were made in regard to the ethereal, preformed, and total sulphates in the urine and will be mentioned later. This will be designated Period 1.

At the completion of the observations she was placed upon the following:

6.30 A.M.: Milk, 200 c.c.

Breakfast, 1 apple; 1 piece toast; milk, 200 c.c.

10.30 A.M.: Milk, 200 c.c.

Dinner: Milk, 200 c.c.; 3 tablespoonfuls of tomatoes; lettuce (plain with salt).

Supper: Milk, 200 c.c.; 1 piece of toast; 3 tablespoonfuls of stewed fruit.

8 P.M.: Milk, 200 c.c.



FIG. 2.—Right hand of Case VIII. Before treatment.

This yielded in the neighborhood of 1375 calories or 10 calories per pound of body weight or 22 calories per kilo. This is near the low limit assigned by physiologists.

The additions to and changes in her diet together with the progress of the ease were as follows:

February 14, 1913. Lettuce, with salt, at lunch.

February 20. Tomatoes (stewed without sugar), spinaeh, and stewed celery (no flour) alternated at lunch.

February 23. One soft-boiled egg added at lunch.

February 27. French dressing on salad.

March 12. Soft-cooked egg at breakfast and supper.

March 31. Stopped evening egg and replaced it by a weighed amount of chicken.

April 21. Baked potato of 150 grams, with 5 grams of butter added once a day at lunch, milk, 200 c.c., stopped and 2 tablespoonfuls of 20 per cent. cream added to the milk twice a day.

April 24. Asparagus. Exchanged meat for the egg at lunch.

The daily ward notes here follow:

February 9, 1913. No essential change in her condition since being upon a house diet for three weeks past.

February 13. New diet started.

February 15. Hands seemed somewhat more wrinkled, the skin being loose; there was less pain on pressure. Had pain in right knee, but slept better than she had been sleeping; pain generally awoke her.

February 18. Hands distinctly better. Skin more wrinkled and knuckles showed when a fist was made. Had a good night. Her period was due in two days, but she had no marked increase of pain and malaise as had been her unusual experience. Right knee was a little better.

February 27. Continued subsidence of swelling. Bony parts were more prominent. Fingers were more spindle-shaped. Period long overdue.

March 3. Period arrived in force. Joints felt fairly well.

March 13. Could have the terminal phalanx of her little finger moved passively for the first time in four years. Right knee was easier in walking.

March 22. Could straighten out right elbow for first time in eight years.

March 28. Marked subsidence of left hand especially, and fingers were more tapering. Period now on, and some pain, but less than usual. Felt great relief in the cervical spine as to mobility and pain.

May 21. Except for the ulnar deviation the left hand almost resembled a normal hand, so great had been the subsidence of the soft tissue involvement and the return of function. The terminal phalanx of the little finger of the left hand, mentioned previously as apparently ankylosed in flexion for four or five years, recovered considerable motility some weeks previously. It was found, however, that it could also be straightened to very nearly the

normal position in extension. The patient's improvement had been so great that it was difficult to appreciate the degree of deformity originally present. Every diseased joint had shared in this, though it was more obvious in some than in others.



FIG. 3.—Hands of Case VIII. After treatment. Notice lessened ulnar deviation, better position of bones in the metacarpophalangeal and wrist-joints, and the lessened soft tissue swelling of right hand as compared with the earlier picture.

June 8. In excellent shape. Hands were better than in last note. On May 13 her dietary, etc., was ample, and consisted of the following, as copied from the record of that day. It varied slightly as above indicated in the list of dietary additions and options:

6 A.M.: 1 glass of milk (200 c.c.).

Breakfast: 1 apple, 120 grams; 1 glass of milk; 1 piece of toast, 24 grams; butter, 11 grams; 1 soft cooked egg, 46 grams.

10 A.M.: Milk (200 c.c.), with 2 tablespoonfuls of cream, 20 per cent.

Lunch: Baked potato, 150 grams; butter, 5 grams; roast beef, 70 grams; raw tomato, 95 grams; lettuce, with 1 teaspoonful of vinegar and salt. (She did not care for oil.)

3.30 P.M.: Milk (200 c.c.), 1 glass, with 2 tablespoonfuls of 20 per cent. cream

Supper: Chicken (stewed), 30 grams; 1 slice of toast, 25 grams; butter, 2 grams; 1 glass of hot milk (200 c.c.); 3 tablespoonfuls of unsweetened prunes.

8 P.M.: 1 glass of milk (200 c.c.).

Her weight at this time was 127½ pounds and she still looked needlessly stout. Practically speaking, she was cured, as the gap to be bridged between this condition and complete recovery was trifling especially as compared with that between her present and her original state, and was seemingly a question only of continuing treatment. Marked pressure over her hand joints still elicited some tenderness, and she complained of some scattered pain at times, but both were growing daily less. The patient went out for a walk every day, and she was active in and around the ward. On July 2 she went home, looking and feeling very well, and still progressing.

CASE IX.—Mrs. F. E., aged thirty-nine years, white. Referred by Dr. William B. Cadwalader, of Philadelphia, from the Orthopaedic Hospital. This patient was a Russian Jewess, and spoke English imperfectly. Her husband and two daughters were healthy, but her previous medical history was not clearly obtainable. Her present trouble dated back nineteen years to Russia, and began in her hands. The shoulders, knees, and elbows became progressively involved over a period of five years, and had grown worse.

She first had a physician for one year at her home, then went for two months to take the "cure" at Odessa, Russia. She was slightly improved by this, but relapsed.

She again consulted her physician, who advised a return to Odessa for two months, but this was without improvement. She then sought other medical advice, came to America, and for two years remained in *statu quo*, but again gradually grew worse. Three years ago she took treatment for one year twice a week at a private hospital, and had Turkish baths, baking, massage, and (apparently) passive hyperemia. This was of no avail, and about one year ago she went to Mt. Clements, Michigan, and took forty-two baths over a period of two months, but says she felt worse as a result of them.

Physical examination revealed a spare woman, somewhat "hunched up," with her right forearm ankylosed at right angles and her left limited in its motion to one-third the normal range. The right wrist was entirely ankylosed and the left practically so. The arms could not be raised at the shoulders, and the hands

showed great lateral deviation, with marked flexion and rigidity of nearly all fingers, though they presented relatively little soft tissue swelling. The synovial sacs of the joints were distended, but the periarticular tissues were so slightly swollen that it seemed that improvement would be difficult of observation until well under way. Her knees and feet were also enlarged and deformed though she was able to walk.

The urine was essentially normal, and the indican reaction was persistently negative. Blood examination showed red-blood cells, 4,420,000; white-blood cells, 10,100; hemoglobin, 60 per cent. The blood-pressure was 112 systolic and 70 diastolic. The heart and lungs were normal.

The x-rays showed the colon to be very long, with the transverse portion ptosed and tortuous. The hands showed chiefly great atrophic and absorptive changes, with some slight hypertrophy.

Upon admission to the hospital she was placed upon the house diet to determine her accustomed food intake, which was found to be about 2053 calories or 20.3 calories per 1 pound of body weight or 44.7 per kilo.

March 9, she was placed upon the following diet:

6 A.M.: 1 glass of milk, 200 c.c.

Breakfast: 1 egg; 1 glass of milk, 200 c.c.; one-half slice of toast; butter, 10 grams.

10.30 A.M.: 1 glass of milk, 200 c.c.

Dinner: Milk, 200 c.c.; spinach, 2 tablespoonfuls.

3.30 P.M.: Milk, 200 c.c.

Supper: One-half piece of toast; lettuce; milk, 200 c.c.

8 P.M.: Milk, 200 c.c.

This yielded about 1375 calories or 14 calories per pound of body weight or 31 calories per kilo. Her weight was 100 pounds.

The additions to and changes in her diet were as follows:

March 17, 1913. One soft-boiled egg at each meal.

March 20. Stopped egg at lunch and supper.

March 21. Stopped milk at 6 A.M. and added 2 tablespoonfuls of cream to the milk at 10 A.M. and 3 P.M. Weight, 98 pounds.

April 4. Stopped milk at 8 P.M.

April 22. Added one-half slice of toast and 2 grams of butter at lunch.

April 25. Added tea, f3j,¹¹ with sugar, 5ij, and 20 per cent. cream, f3iv, once daily; baked potato, 150 grams, with 5 grams of butter once daily; stopped 1 glass of milk.

April 27. Added 15 grams of butter daily.

May 3. Added 1 apple at breakfast and supper.

May 18. Patient's diet was as follows:

¹¹ Since many of the ward directions were more conveniently given in tea- and table-spoonfuls, their familiar equivalents in f3 and f3 were sometimes used.

Breakfast: 1 soft-boiled egg, 50 grams; 1 glass of milk, 200 c.c.; $\frac{1}{2}$ slice of toast, 15 grams; butter, 2 grams; apple, 100 grams.

Dinner: 1 cup of weak tea made thus: f3j of tea, with f5iv of 20 per cent. cream and 5ij of sugar (two teaspoonfuls), balance of hot water; $\frac{1}{2}$ slice of toast, 15 grams; 3 tablespoonfuls of tomato; roasted potato, 150 grams; butter, 20 grams.

Supper: $\frac{1}{2}$ slice of toast, 15 grams; butter, 2 grams; lettuce, with 2 tablespoonfuls of French dressing (one part of vinegar to three parts of oil); 3 tablespoonfuls of unsweetened prunes (or other cooked fruit); 1 apple, 90 grams.

March 13. Diet started March 9. Had considerable pain at night. Made little complaint.

March 14. Better night.

March 16. Apparently definite signs of improvement in laxity of joints, depressions over joints, and freedom of movement (active and passive) of small joints.

March 17. Could reach her head with her left hand. This was impossible for three months before. First finger of right hand could be better abducted. One egg added to lunch and supper.

March 20. Had three eggs for three days. Improvement very doubtful, though tendons on back of hands seemed to stand out better. Seemed to make better progress on lower diet. Stopped two eggs.

March 21. Not well and having pain. Joints no better. Stopped one glass of milk and added two tablespoonfuls of cream to 10 A.M. and 3 P.M. milk.

March 26. Much improved. Distinct laxity and mobility of joints.

April 2. Had sharp tonsillitis, with fever. Better, but still some fever. Hands showed improvement. Were stiff and painful during her febrile period.

April 4. Still had fever and much pain. No great change in joints, though slightly in direction of improvement. Given aspirin, gr. xv, at once, and in two hours, and then gr. x every four hours for relief.

April 5. Had relief from the aspirin. No other change.

April 6. Fingers better. Temperature normal. Aspirin stopped.

April 7. Could move her shoulders better, and also straighten out her hands. Temperature was normal, but recent "grippe" had caused her to lose weight. Not getting aspirin, and is very happy.

April 8. Better than at any time yet. "I feel fine." Moved shoulders and moved and supinated forearm better than for three to four months. Almost no pain in knees, and felt better.

April 10. Stiffer in elbows and knees, though both moved. Was well on previous day.

April 21. Steady improvement. Whole personality had grown brighter. Hands could be considerably straightened.

April 24. Felt well and wanted to get up.

May 3. Added one apple to breakfast and to supper. Doing very well.

May 8. Very well previous day. Felt stiffer, as did several other joint cases in the ward, coincidently with a change in the weather. Slight swelling of feet on previous day. Slightly better. Had pain in muscles of back in the night.

May 11. Much better. Was doing very well.

May 16. Thought she had been stiffer at night lately and had more pain then. Joints showed only improvement on inspection, however.

It was difficult in this case to differentiate between the pain due to contracted tendons and that of joint disease *per se*. She complained greatly of pain, especially at night, though objectively she seemed to improve. Her diet had been decreased and increased at various times until, on June 19, she received the following, with slight daily variations:

Breakfast: 1 egg; toast, 18 grams ($\frac{1}{2}$ slice); 1 glass of hot milk, 200 c.c.; butter, 2 grams.

10 A.M.: 1 glass of milk, 200 c.c., with 1 tablespoonful of 20 per cent. cream.

Dinner: 1 baked potato, 150 grams; turnips, 3 tablespoonfuls, or some other green vegetable as noted elsewhere; 1 tomato; 1 cup of weak tea, with 1 tablespoonful of 20 per cent. cream, and 1 teaspoonful of sugar; butter, 20 grams; 1 apple.

4 P.M.: Milk, 200 c.c., with 1 tablespoonful of 20 per cent. cream.

Supper: Toast, 15 grams ($\frac{1}{2}$ slice); butter, 2 grams; unsweetened stewed fruit, 3 tablespoonfuls; hot milk, 1 glass, 200 c.c.; lettuce, with 1 tablespoonful of French dressing, 1 to 3.

Her complaint of pain was so persistent that her diet was reduced on June 23 by stopping the potato and butter at dinner and the milk at 10 A.M. and 4 P.M. On June 25 and 26, the pain was distinctly less. On June 28 it was noted that she walked better than at any time to date, and she said that she could comb her hair and dress herself more easily than she had been able to do for some time. Her joints felt well and limber, but the muscles felt sore from calisthenics and passive movements.

This was one of the most difficult cases to handle. The duration of her illness, nineteen years, the advanced degree of contractures, the intensity and frequency of pain, often made her progress seem slow or doubtful, even though the objective signs were favorable. As in some other cases, the disease eventually was apparently arrested, and the problem became one largely of the mechanics of the joints.

On July 1 she was practically free from pain, her only complaint being that she wanted more food, and was discharged, with in-

structions to continue her exercises and keep to her diet. She could attend to all her wants in dressing and every-day acts.

It will be seen that this case represented the most advanced and longest standing type of the disease, and was deliberately treated as a test. To undo the structural injury of so many years was of course impossible, the idea being to determine whether the disease was amenable at all when so firmly established. It was plain that it could be arrested, but only at a low level of food intake, as the gaps in the "metabolic chain" become perhaps wider after long duration. The patient grew restive under a low dietary, and on returning home she was reported to have considerable discomfort.

CASE X.—Miss H., aged twenty-four years, nurse—attendant at the Country Home for Convalescents of the Presbyterian Hospital of Philadelphia. She presented a history of having had an attack of rheumatic fever when aged thirteen years, at which time many joints were involved, and she was ill for two months. Practically every winter since then she had had, between December and February, a recurrence of rheumatism, especially in her knees and ankles. At these times the joints were painful and usually swollen. The attacks lasted from two weeks to one month, though pain in the joints was noticed for weeks afterward.

The patient had an attack of tonsillitis when aged ten years, and in 1911 an outbreak of rheumatism following the latter.

Since January, 1911, she had had more or less persistent pain and grating in both ankles at all times.

Physical examination revealed a slight goitre, unassociated with tachycardia, exophthalmos, tremor, cardiac hypertrophy, or nervousness, which had been present and constant in size for many years.

The phalangeal joints of her hands were slightly enlarged. The left ankle was tender on pressure, and active or passive motion of either the right or the left ankle gave a slight grating which could be heard and felt. Blood and urine were normal. Weight on admission to the hospital was $101\frac{1}{2}$ pounds in her night-dress.

The x-ray examination showed the colon to be elongated and sharply flexed at the hepatic and splenic flexures. The hands showed slight but definite hypertrophic and atrophic changes. The patient's best weight had been 115 pounds.

On November 19, 1912, she was placed tentatively upon a slightly modified diet, as follows:

Meat for dinner only and in very moderate amounts. No potatoes or rice and very little bread; six glasses of milk per diem, distributed at 6 A.M., breakfast, 10.30 A.M., lunch, 3.30 P.M., and at supper. Green vegetables were allowed *ad libitum*. Her weight was $109\frac{1}{2}$ pounds in her clothes.

The notes made in the Presbyterian Hospital dispensary, which she attended, were as follows:

January 8, 1913. Was on night duty and lost nearly two pounds. Took cascara at night, as she was rather costive. Had no rheumatism at all, and had not been free from it for so long a period during the past year. Diet at this date: 6.30 A.M., 1 glass of milk. 8 A.M., breakfast, 1 glass of milk, 1 small slice of toast, 1 egg or small amount of fish or scrapple or (rarely) hot cakes. 10.30 A.M., 1 glass of milk. Dinner, 1 P.M., clear soup, 1 glass of milk; meat in moderation, green vegetables, no rice or potatoes. Custard or junket or wine jelly for dessert, but no bread or rice or flour puddings. 3.30 P.M., 1 glass of milk. Supper at 6 P.M., 1 glass of milk, lettuce, stewed fruit, or jelly; occasionally a small amount of scrambled egg. Weight now 108 pounds.

January 22. Beginning ten days previously and until the day before had pain in ankles, shoulders, knees, wrists, and right elbow. Weight, $108\frac{1}{4}$ pounds. Desserts and meat at dinner were stopped. Advised to rest one hour in morning and afternoon.

January 28. Much better, except that her feet were not much improved. Tongue clean. Bowels open. Weight, $108\frac{1}{4}$ pounds.

March 5. Feeling "fine." Two weeks before, patient had some pain and stiffness in the left shoulder for one day and one night. The proximal point of the third finger of the left hand was slightly stiff off and on for several days at the same time. She had been entirely free from headache for six weeks; formerly was subject to it oftener than that.

March 17. Ten days previously had a bilious attack, with vomiting, and began to have pain in right wrist, thumb, and two fingers. Patient was given two doses of aspirin, each ten grains, by the resident physician, before consulting the writer after which her diet was ordered somewhat reduced, and she was put to bed and given calomel and salts. She had no other antirheumatic or analgesic medicine, and after four days in bed, where she was kept to avoid undue tissue loss during the low dietary, she went back on duty and had been active and "feeling fine" for four days.

April 18. Apparently perfectly well, and had been on night duty for a month or more. Weight, $106\frac{3}{4}$ pounds. Was not taking medicine of any kind.

June 18. Patient was sent for and found to be feeling well, performing the regular hospital duties, as she was also on July 1.

(To be continued.)

REVIEWS

ANATOMY, DESCRIPTIVE AND APPLIED. By HENRY GRAY, F.R.S., Fellow of the Royal College of Surgeons; Lecturer on Anatomy at St. George's Hospital Medical School, London. New (American) edition, thoroughly revised and re-edited, with the ordinary terminology followed by the *Basle Anatomical Nomenclature* by EDWARD ANTHONY SPITZKA, M.D., Director of the Daniel Baugh Institute of Anatomy and Professor of General Anatomy in the Jefferson Medical College of Philadelphia. Pp. 1502; 1225 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THE new American edition of *Gray's Anatomy*, representing the nineteenth edition, will unquestionably be welcomed by a large proportion of the students and teachers of this subject. For half century or more the work, both in the original and the many succeeding editions, has been held in high repute as a thoroughly practical treatise.

In comparing this edition with the preceding one which was published in 1910 no very great changes will be noted. About 20 or 25 new illustrations have been added, a few unessential details eliminated and only such additions made as were necessary to represent the recent anatomical advances. Many points may be cited in praise of the book. Every effort has been made by both the eminent revisionist, Dr. Spitzka and the publishers to make the book fulfil every requirement for which it was intended and to maintain the high standard which has characterized the book in the past. The subject of human anatomy is presented in as broad a manner as possible without endangering its usefulness as a text-book for the student. The text throughout is clear, concise, systematic and the abundant use of superb illustrations, in colors, cannot fail to be appreciated by the reader. A good feature of the illustrations is the printing of the names of the parts directly on them. It assists one in remembering the location and relations. Recognition of the increasing use of the *Basle Anatomical Nomenclature* has been indicated by following the ordinary terms which are familiar to American students with the B.A.N. terms in parenthesis. The new terms are also italicized in the index.

The sections on osteology, syndesmology and myology are very thorough; the illustrations of the first mentioned section have the museular attachments outlined in red and those of the capsular

ligaments in blue. The description of the muscles is facilitated by plates showing the attachments in red and the insertions in blue. Much space has been devoted to the consideration of the vascular systems which are given in detail. The nerve system is carefully and faithfully described and the practical manner in which it is presented will materially assist the beginner in acquiring a knowledge of the rather intricate morphology of the central nerve system. A more detailed description of the course of the superficial nerves would be an improvement and of great help to surgeons who are desirous of using Kocher's method of conduction anesthesia or the "nerve-blocking" method advanced by Dr. Cushing. Greater knowledge of the nerves, for many reasons, is becoming more and more of a necessity to the surgeon and it is a noticeable fact that nearly all of the present day text-books are deficient in this regard.

The organs of special sense, digestion, respiration and of the uro-genital system are described in a complete, comprehensive manner and the text is free of obscure or perplexing passages. Instructions for dissecting are given at intervals throughout the book, and while very meager will be of use to the student.

Histology and embryology are considered briefly, short accounts only being interpolated in connection with the gross anatomy of the various structures. Under the title of Applied Anatomy many surgical and medical conditions are discussed, and while helpful otherwise emphasize the importance of a thorough, practical knowledge of anatomy in the practice of modern medicine and surgery.

All things considered this edition is a decidedly attractive one and will probably meet with even greater demand than its predecessor.

H. D. L.

A MANUAL OF OTOTOLOGY. By GORHAM BACON, A.M., M.D., Professor of Otology in the College of Physicians and Surgeons, Columbia University, New York. New sixth edition. Pp. 536, 164 engravings and 12 plates. Philadelphia and New York: Lea & Febiger, 1913.

DR. BACON'S *Manual of Otology*, now appearing in its sixth edition, is well deserving of its popularity, as it contains more concise information about the ear than any other work of its size and character. It is undoubtedly the best known manual of diseases of the ear in America, and the present edition is well edited, with many sections rewritten and enlarged, while new ones have been added to keep pace with the growth of knowledge in otological subjects since the last edition appeared. So well known is the book that it hardly seems necessary to go into its merits in

great detail. There are, however, some particulars in which the reviewer feels that it could be still further improved.

The sections on the anatomy and physiology of the ear are well written for the most part and clear; well illustrated with schematic drawings and photographs of gross temporal bones and histological sections. At the present time, when the labyrinth is so much under discussion and so much research work is being done on its physiology, it would seem that the description of its anatomy, difficult for a tyro to understand at the best, might be clarified and simplified.

Excellent are the illustrations throughout, the well-known ones being supplemented by many new ones, mostly photographs of actual specimens. In this connection it would seem that the modern custom of putting in plates of sets of instruments necessary for a given operation might well be changed and the space taken up with these somewhat useless illustrations, used for more text.

Dr. Bacon's admirable conservatism is apparent throughout the book, which is brought up-to-date by the addition of the latest knowledge of labyrinth reaction tests and operative procedures. This latest edition deserves, as all previous editions have deserved, its rank as a standard manual and should be on the shelves of every practitioner of medicine who wishes condensed information on diseases of the ear.

G. M. C.

MINOR AND OPERATIVE SURGERY, INCLUDING BANDAGING. By HENRY R. WILARTON, M.D., Surgeon to the Presbyterian Hospital, Children's Hospital, Consulting Surgeon to St. Christopher's Hospital, etc. Eighth edition; pp. 700; 570 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THE fact that this work has reached its eighth edition is evidence of its popularity. The greater part of the text is accurately to the point and gives the desired information in the shortest space possible. However, at times the author wanders aside from his chosen field into the realms of bacteriology and literature. Again, some of the simpler elementary subjects are dealt with a little too exhaustively; a good point, however, if not carried too far. On the other hand, there is no mention of some important minor subjects, such as the technique to be followed in the search for a foreign body in the soft parts.

The illustrations are very numerous. It should be noted, however, that several of the illustrations of bandages are incorrectly drawn by the artist; a point of importance only from a student's standpoint.

In the operative chapter the author has treated as minor procedures a number of operations that are generally conceded to be

major work, such as nephrectomy, ureter surgery, pyloroplasty, etc. Such minor procedures, however, as removal of a sebaceous cyst, or a foreign body under the nail are not mentioned. Aside from these criticisms, which are perhaps largely a matter of individual opinion, the work has many good points and in the future, as in the past, will doubtless prove of value to many. E. L. E.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago, August, 1913. Vol. II, No. 4; Pp. 104; 50 illustrations. Philadelphia: W. B. Saunders Co., 1913.

THIS number opens with a paper entitled "Some Observations on Vaccine and Serum Therapy from Dr. Murphy's Clinic," by Philip H. Kreuscher, M.D., of Dr. Murphy's Staff. The paper was read before the South Side Branch of the Chicago Medical Society, May 27, 1913, and it is followed by the discussion which took place when the paper was read, participated in by Dr. Charles L. Mix, Dr. T. L. Dagg, Dr. J. L. Miller, Dr. L. Hektoen, and Dr. Murphy himself. Dr. Murphy's views on the subject are further expounded in two clinical lectures delivered at Mercy Hospital during the following week. The entire discussion on vaccine and serum therapy thus occupies a space of 35 pages. The conclusion of the whole matter seems to be that in acute infections the use of sera is more efficacious than is that of vaccines, because the patient is thus supplied with ready-made antibodies; but in chronic infections, where there is time to stimulate the patient's own powers of antibody production, vaccines may prove of considerable benefit, especially if the infecting organism is known. Dr. Murphy and his staff have used them chiefly in cases of chronic joint disease, and their beliefs are thus stated by Dr. Mix: "From the date of the original infection and the date of the appearance of the metastases in the joint, the physician may be able to name the germ. Recall, for example, typhoid fever—when do the joint disturbances begin? In the third or fourth week. When do the joint disturbances after the period of acute infection in gonorrhea begin? In our experience the joint becomes infected only between the eighteenth and the twenty-second day. When do the joints become infected in the streptococcic infections? In our experience the second or third day. Each of the germs more commonly at fault in the joint infections has a definite time for infecting the joint after the primary infection" (p. 561). It is further stated by Dr. Mix that where the infecting organism is not known, "mixed vaccine therapy is in accordance with common sense:" but Dr. Hektoen (p. 565) cautiously says "as regards the use of mixed

vaccines, it does seem to me that we ought to proceed very slowly and very carefully. It may be perfectly proper to use mixed vaccines, provided we are certain we have a mixed infection."

There is next presented a series of ten radiographs of the larger joints of the body (most of them shown in two planes) made after injecting the arteries with a red-lead emulsion. Professor Ranson of the Department of Anatomy of the Northwestern University Medical School made the cadaveric preparations, the skiagraphs were made by Dr. George W. Hoebrein "who does all the radiographic work for Dr. Murphy," and the illustrations were properly labeled with the names of the arteries and their branches by Mr. Sumner Koeh, an assistant of Professor Ranson. These illustrations are of great interest and considerable value, though the injected vessels naturally appear to lie all in one plane.

The main bulk of the volume is made up, as usual, of clinical talks by Dr. Murphy, covering a wide range of topics, in which bone surgery holds the most important place. But the concluding article (for it is not a clinical lecture, nor has it "never appeared in print before") is on appendicitis, or rather "On early operation in perityphlitis," being an abstract of a paper published by Dr. Murphy, February 26, 1890; it is "reprinted to show striking similarity between Dr. Murphy's teaching of today and that of twenty-five years ago." For all of this let us be duly thankful.

A. P. C. A.

SYPHILIS AND THE NERVOUS SYSTEM. By MAX NONNE, Chief of the Nervous Department of the General Hospital, Hamburg. Authorized translation from the second revised and enlarged German edition by CHARLES BALL, M.D., Chief of the Nervous and Mental Department of the St. Paul Free Dispensary. Pp. 406; 98 illustrations. Philadelphia and London: J. B. Lippincott Company, 1913.

It was a happy idea which caused Dr. Ball the translator, to bring to the English speaking physicians Nonne's excellent book on syphilis and the nervous system, for there is no one physician who has had such wide opportunities nor is there one who has had more skill and aptitude for this kind of work than he. Perhaps there is no division of medicine which is undergoing such changes so far as classification is concerned than the specialty of nervous diseases and a large part of it is due to the fact that we are gradually recognizing that many more diseases of the nervous system are due to syphilis than we originally thought. In the recognition of syphilitic diseases of the nervous system the greatest help has been the so-called four reactions of Nonne, the author of this book.

The present problem deals not so much with the clinical phases of the subject, as with the question of whether we should continue the old classification of meta-syphilitic diseases, and their therapy. Nonne in a recent paper before the International Congress in London took the attitude that we are unable at the present moment to say definitely what is a meta-syphilitic disease and what is not, and the only thing we can definitely say is, that syphilis causes this and that disease, and that the best thing to do is to wait and see what further advances will teach. As far as the therapy is concerned, he states that he is not as hopeless regarding the therapy of tabes as others are, for he himself has seen four cases in which the Argyll-Robertson pupils have disappeared under mercury and salvarsan. The reviewer can only repeat that this is the best book on syphilis of the nervous system and the translator has done his work well.

T. H. W.

TEXT-BOOK OF GENERAL AND SPECIAL PATHOLOGY, FOR STUDENTS AND PRACTITIONERS. By HENRY T. BROOKS, M.D., formerly Professor of Pathology at the New York Post-Graduate Medical School and Hospital. Pp. 1127; 525 illustrations (110 in colors) and 15 plates in colors. Philadelphia: F. A. Davis Company, 1912.

THIS book was started as a translation of Langerhans "Grundriss der Pathologischen Anatomie," but advances in the science and the death of the German pathologist caused the author to adopt another method in the preparation of his book. The work is intended to follow the pathological physiology through the various evidences of disease, physical changes being traced as evidence of these altered processes. The book is not a physiological chemistry but the metabolic reasons for the pathological states are emphasized. Minute pathology is more extensive than the gross which is given in a sketchy manner. The author aims at assisting the student and the physician in the interpretation of clinical conditions. The first half is devoted to the broad principles of pathology, the second half to special organs. In the first part considerable attention is given to peculiar manifestation of the different diseases in special organs. Similar treatment is found under inflammations. The chapters on immunity and on the eye are by collaborators. The latter is, in length, out of all proportion to the rest of the book occupying 150 pages while the vascular system is accorded less than 40. The result is, however, a fairly complete, condensed, and readable pathology of the eye, a thing uncommon in most one-volume general pathologies. The method of spelling all adjectives and adverbs such as clinical and clinically without the "al" seems to the reviewer to be not wholly advisable. "Clinic" and "clinically"

are especially awkward. The illustrations are mostly copied and the one-toned colored pictures are sometimes indistinct. The schematic originals intended to show certain physical relations of disease are much better. The English reads easily except for the form of adjectives noted above. On the whole, in spite of the large number of general pathologies that already exist, the book should prove of value.

H. F.

TEXT-BOOK OF OBSTETRICS. By BARTON COOKE HIRST, M.D., Professor of Obstetrics in the University of Pennsylvania. Pp. 1013; 895 illustrations. Philadelphia and London: W. B. Saunders Co., 1913.

VERY little that is new has occurred in obstetrics since the previous edition, but those procedures that have any bearing upon modern obstetrics are embodied in this work. The author is most enthusiastic about the close relationship of obstetrics and gynecology, and many so-called gynecological operations are described in detail. The physiology of the process of generation precedes the pathology, except that sterility is taken up in connection with normal conception and malpositions, and presentations are studied with the mechanisms of labor. The pathology of the breast is treated more fully than in the previous edition; especially is this true of malignant disease. There are also many new illustrations which aid materially in teaching. The author comments more favorably in this edition, upon extra-peritoneal Cesarean section, and thinks its field has enlarged. It is generally believed, however, that suspect and infected cases had best not be subjected to any method wherein the uterus is opened, intra- or extra-peritoneally, and allowed to remain after the child is removed.

The author's practice of delaying repair of a primary laceration of the perineum until the end of the first week, has not met with the approval of the majority of obstetricians. A second etherization and disturbance of the patient just when conditions are resuming the normal, seem unwarranted, when one considers the good results obtained by an immediate repair.

The author has commented freely upon the newer ideas in obstetrical teaching, such as the use of the active principle of the pituitary gland in uterine inertia, the significance of the changes in blood pressure in toxemias, serum therapy in puerperal infections, the inadvisability of doing hysterectomy in early puerperal infection, and the excision of thrombosed pelvic veins. His teaching on all these subjects is conservative and sound. The work is most readable, the subjects are disposed of in a clear, concise, and up-to-date manner, equally valuable to pupil and general practitioner.

E. P. B.

DISEASES OF THE EYE. A HANDBOOK OF OPHTHALMIC PRACTICE FOR STUDENTS AND PRACTITIONERS, By G. E. DE SCHWEINITZ, A.M., M.D. Professor of Ophthalmology in the University of Pennsylvania, and Ophthalmic Surgeon to the University Hospital; Consulting Ophthalmic Surgeon to the Philadelphia Polyclinic; Ophthalmic Surgeon to the Philadelphia Hospital; Ophthalmologist to the Orthopedic Hospital and Infirmary for Nervous Diseases. Seventh edition; pp. 979; 360 illustrations and 7 plates. Philadelphia and London: W. B. Saunders Co., 1913.

IN the twenty-one years that have elapsed since its first appearance, there have been seven editions and several reprints of de Schweinitz's treatise. This shows clearly what the profession thinks of it. It is not too much to say that it is the American text-book *par excellence* and will hold its own with any similar work in any language. A complete and well arranged index of 56 pages adds to the value of the book.

The present edition differs from its predecessors in careful revision of the subject as a whole, and in the addition of such recent contributions as are likely to obtain a permanent place in ophthalmology. These include, among others, a short description of the tonometer, particularly that of Schiötz, to replace the finger test which is declared to be neither a safe nor an accurate procedure; Hertzell's diaphanoscope and the manner of using the same is described, together with the appearances it gives of the interior of the eye, especially in connection with orbital and sinus disease. Elliot's operation of trephining of the sclera in glaucoma is summarized, as is also Toti's operation in disease of the lacrimal sac, and Reese's muscle resection operation. Recent descriptions of certain ocular affections, such as sporotrichosis, Widmark's conjunctivitis, blue sclerotics, von Hippel's disease, etc., are alluded to.

Salvarsan and neosalvarsan are highly recommended in syphilitic iritis; the author's experience has shown excellent results from the administration of gonococcic vaccine in gonorrheal iritis, which form the writer has found much more common than has usually been supposed, this being the origin in many instances of so-called rheumatic iritis.

Of the Smith or Indian method of extraction of cataract in the capsule, the author quotes a brief description; he gives it as his impression "that while this operation may have a place in ophthalmic surgery, especially in the extraction of unripe cataracts, it is not likely to drive from the field those procedures which have for years been firmly and favorably established."

As the reviewer stated upon the occasion of a review of an earlier edition of this work, this hand-book is an entirely reliable and satisfactory account of the present position of ophthalmic science.

As pointed out by Hirschberg, it has a certain advantage over larger and encyclopediae treatises, in that it is practically the outcome of a single mind, "von einem Guss." It has another quality by no means always found in scientific, particularly medical, writing: the style is precise and clear and makes easy reading, and we know from an eminent writer that "easy reading is hard writing."

The work will no doubt continue to meet with the same cordial reception which has been accorded to its predecessors.

T. B. S.

PATHOLOGY. A MANUAL FOR TEACHERS AND STUDENTS. W. T. COUNCILMAN, M.D., Shattuck Professor of Pathology, Harvard Medical School. Pp. 405. Boston: W. M. Leonard.

THIS manual is an extension of the syllabus of Pathology published by Councilman and Mallory in 1904 and is designed with special reference to the teaching of the subject. Illustrations are purposely omitted to encourage the student to make his own illustrations from actual specimens and for this purpose, in addition to the 405 pages of text, 263 blank pages are introduced at the end of the various chapters. There is considerable difference in the fulness with which different subjects are discussed. Inflammation and repair are treated rather completely. The entire subject of tumors is covered in 40 pages. Under the infectious diseases the lesions usually resulting from twenty-four of the commoner organisms are described, occupying in all 135 pages. To parasitic worms 4 pages are given. The pathology of the kidneys is considered at especial length. The classification of the nephropathies is exceedingly clear and simple and emphasizes the histologic rather than the gross changes in these organs. On the other hand, the discussion of hepatic conditions, notably the cirrhoses, is very brief and incomplete. The author states that the variation in the space allotted to various subjects is not meant as an index of their relative importance, but that fuller description is given to those conditions which illustrate principles of wide application. Following almost every chapter is a description in outline of experiments which the student may perform, illustrating the principles and conditions that have been studied. This feature of the book, comprising in all about 50 different experiments, has been prepared by Assistant Professor Karsner and adds much to its value. After the discussion of the special pathology of each system and of each of the common infectious diseases the author has added full illustrative autopsy protocols, sometimes with the clinical history of the case. These protocols, of which there are 54 in all, are followed by a few critical remarks. The book seems to us to be exceptionally well adapted to the purposes for which the author intended it.

J. H. A.

THE TREATMENT OF DISEASES IN CHILDREN. By G. A. SUTHERLAND, M.D., F.R.C.P., Physician to Paddington Green Children's Hospital. Second edition. Pp. 403. London: Henry Frowde, Hodder, & Stoughton, 1913.

THE book is designed as a practical guide in treatment for the young practitioner. The necessary descriptions of the various diseases are concise, conservative, yet contain all the facts that may be safely accepted or the most plausible theories in lieu of facts. The author wisely adopts the plan of describing in full one definite line of treatment rather than enumerating long lists of remedies or measures which have attained more or less reputation as cures in the diseases discussed. The chief impression upon reading the book is that it is written by a pediatrician of sound views and admirable common sense, who knows whereof he writes. For example, the results of a careful personal observation of over 100 cases of orthostatic albuminuria are worthy of careful attention. The book, therefore, represents a real addition to the knowledge of practical treatment, not merely a skilful compilation of heterogeneous opinions.

It will suffice to point out the comparatively few instances where his teaching differs from that of most American authors. The dosage of some drugs is larger than we usually accept as desirable. The diet provided for patients with typhoid fever falls far short of average caloric requirements and is distinctly less than modern American practice accepts. The open air treatment of cases of marasmus with subnormal temperature, is being replaced in many American hospitals by the use of superheated rooms, with results which scarcely permit of doubt as to their efficacy. In the matter of general dietetics, it often seems that English children are more fortunately equipped, in a gastronomic sense, than their American cousins. Certain it is that the most conservative English pediatricians are more liberal in feeding children than their American confrères, while their precaution in the use of flannel "next to the skin," during the summer, in such diseases as rickets, must be due to climatic conditions as well as to conservatism. The suggestion that the superfluous fat seen in many rickety babies tends to prevent free cutaneous circulation and should be reduced by restricting carbohydrates in the diet, has much to recommend it. Another suggestion, new to the reviewer, is that cases of chronic intestinal indigestion and marasmus, bottle-fed, should receive the benefits of a variety in the twenty-four hours diet; for example, milk mixtures by day and whey at night. Finally the author's views on quarantine in diphtheria will strike a sympathetic chord in the minds of many of his readers. He believes that the persistence of positive cultures four to eight weeks after the inception of the disease—depending upon the type of case—should not restrict the patient to the trying conditions of strict quarantine. J. C. G.

DISEASES OF THE STOMACH AND UPPER ALIMENTARY TRACT. By ANTHONY BASSLER, M.D., Professor of Clinical Medicine, New York Polyclinic Medical School and Hospital. Second edition. Philadelphia: F. A. Davis Company, 1913.

THE compliment of a large first edition exhausted in the first year of publication is almost sufficient in itself to make a review of their book unnecessary.

The work is an exhaustive treatise on diseases of the stomach and the upper alimentary tract, based on facts that have been derived from many years of clinical observation in public and private practice re-inforced by much first-hand laboratory knowledge of the safe and sane kind.

The essential anatomy and histology of the tract is thoroughly covered; there are helpful suggestions regarding the importance of careful history taking and the keeping of permanent records; the sections on etiology, pathology, symptomatology, and diagnosis are clear-cut, comprehensive, and readable, and the several chapters devoted to a discussion of the different forms of treatment, by diet, drugs, waters, electricity, and other physical therapeutic measures, are especially good. For the man doing special work along gastro-enterological lines and for medical students this book can be recommended as one of the best on the subject in the English language within the reviewer's knowledge.

B. B. V. L.

THÉRAPEUTIQUE USUELLE DU PRATICIEN TRAITEMENT DE LA TUBERCULOSE. By ALBERT ROBIN, Professeur de Clinique, Thérapeutique à la Faculté de Médecine de Paris. Third Series; Pp. 640. Paris: Vigot Freres.

ONE approaches with considerable hesitancy a volume of such length on the treatment of tuberculosis, fearing lest in the obvious detail of the many important subheadings the author may have failed to preserve perspective and proportion.

In this work the first fifty pages lead one into such a chaos of chemical and metabolic inaccuracies that one's fears are confirmed and further reading made difficult. It is scarcely necessary to add that the clinical chapters are filled with references to such delightful fictions as the "co-efficient de robusticité de Pignet" and a classification of the liver conditions due to tuberculosis into twelve subdivisions. In the sections which are truly concerned with treatment, every method good or bad is discussed in full. Twenty-five pages are devoted to the cure of tuberculosis by mineral waters, and the serum of Marmoreek receives undue consideration.

The book, as a whole, is distinctly verbose and unscientific, and is a representation of the worst faults of French medical writings.

O. H. P. P.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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On the Infectivity of the Milk of Syphilitic Women.—P. UHLENHUTH and P. MULZER (*Deutsch med. Woch.*, 1913, xxxix, 879) have succeeded in demonstrating experimentally the presence of *Treponema pallidum* in human milk. Of 8 cases studied, positive results were obtained in 2. The milk used in the experiments was sucked from the breasts by means of a Bier cup, the nipple and breast having been previously cleansed with bichloride of mercury. The milk was then injected into rabbits' testicles. P. Uhlenhuth and P. Mulzer emphasize especially the importance of the finding of spirochetes in the milk of the mother of a syphilitic child, the mother being free from symptoms (latent syphilis). The mother's blood gave a positive Wassermann reaction, and they also succeeded in demonstrating the presence of the spirochetes in the blood of a similar case. These facts, therefore, demonstrate the danger of accepting a woman as wet-nurse to non-syphilitic children. The absence of symptoms does not mean that a syphilitic is in a non-infective stage of the disease, and all possible means should be adopted to exclude the disease.

A New Prophylactic Remedy against Diphtheria.—E. VON BEHRING (*Deutsch med. Woch.*, 1913, xxxix, 873) reports his recent studies in the prevention of diphtheria by the use of a mixture of diphtheria toxin and antitoxin. The mixture has been employed in a large series of animal experiments and finally in man by the von Behring colleagues in the Marburg clinics. The mixture of toxin and antitoxin employed is one which is practically non-toxic to guinea-pigs. It is found, however, that this mixture is not inert in all animals. Repeated doses of it may kill an ape, so that the toxin cannot be said

to be neutralized. Toxin and antitoxin given in this proportion, however, is practically non-toxic to man. By injecting small quantities of this preparation a high degree of active immunity may be conferred on patients. It is estimated that sufficient antitoxin units will remain in the blood to confer immunity for a period of two years. It is found, moreover, by obtaining serum from an actively immunized patient and injecting it into a second patient, that the injection of this homologous serum produces an immunity which greatly outlasts that produced by heterologous sera. The remedy is not given out yet for general use. Behring is collecting data from a few clinics. Before administering the serum, the presence or absence of antitoxin in the patient's blood is determined; if present, the quantity of antitoxin is estimated. The presence or absence of diphtheria bacilli in the respiratory passages is also determined. Then after the remedy is given, Behring requires that the quantity of antitoxin units in the patient's blood be determined at intervals for a long period of time and also that throat cultures be examined frequently for diphtheria bacilli. In this way, he plans to obtain exact information as to dosage, reaction, the amount of antitoxin produced in the human blood, and the duration of the protective reaction. When sufficient material has been collected, a further report will be made.

New Preparations and New Principles for the Treatment of Trypanosomiasis.—W. KOLLE, O. HARTOCH, M. ROTHERMUNDT and W. SCHÜRMAN (*Deutsch med. Woch.*, 1913, xxxix, 825) report the results of important studies of the chemotherapy of experimental trypanosome infections. The observations were carried out largely upon mice. The organisms used were the trypanosomes of the sleeping sickness, nagana, and dourine. The authors have found that it is possible to cure experimental trypanosome infections of mice with a single intramuscular injection of metallic antimony as well as with various water-insoluble organic and inorganic preparations of antimony, provided the antimony is in the trivalent form. After the injection of metallic antimony and numerous preparations of antimony, however, the mice died of chronic antimony poisoning. Certain antimony compounds nevertheless, are relatively non-toxic when administered intramuscularly. Of these a 30 per cent. oil emulsion of trioxide of antimony, which the authors designate "trixidin" for the sake of brevity, has proved the most efficient. It is the most active preparation examined, when given intramuscularly. It is found that $\frac{1}{100}$ of the fatal dose is sufficient to cure infections in mice. No evidence of antimony poisoning followed its use. Through one or two intramuscular non-toxic doses of trixidin, sterilization of infected mice is accomplished in 100 per cent. of cases. In its therapeutic index (1 to 100) and in its effectiveness it far surpasses previously studied preparations of antimony. The authors believe it will prove equally non-toxic and useful in the treatment of trypanosomiasis in man. The pentavalent antimony compounds are not only weak pharmacologically and toxicologically, but they are also without any marked therapeutic effect in trypanosome infections. Next the authors tried to find a method of employing trivalent compounds which are too toxic to be safe when given intramuscularly, but which are none the less highly active

against the trypanosomes. They have discovered that these preparations when incorporated in an ointment may be used as an inunction with very good results. Thus, metallic antimony and certain insoluble compounds in the form of a salve may cure infections of mice, rats, guinea-pigs, rabbits, and monkeys in about 66 per cent. of cases without the slightest evidence of toxic action. In contra-distinction to *therapia magna sterilisans* which on account of the large quantity of soluble drug quickly thrown into the circulation is dangerous and which must be repeated at intervals as the experience with salvarsan has shown, the authors designate their antimony treatment, *therapia mite curans*.

Avian Tuberculosis in Man.—E. LOEWENSTEIN (*Wein. klin. Woch.*, 1913, xxvi, 785) reports observations on three new cases of human infection with avian tubercle bacilli. He summarizes his studies as follows: The occurrence of avian tuberculosis in man is probably much commoner than is generally supposed. The cases are characteristic both bacteriologically and clinically. In all cases in which one finds acid fast bacilli, which are non-pathogenic for guinea-pigs, rabbits and chickens should be inoculated, and pure cultures of the organisms should be obtained. A simpler method of identification of the disease consists in the use of the skin test with avian tuberculin. Children infected only with avian tubercle bacilli do not react to human tuberculin but give a marked skin reaction with avian tuberculin. The clinical course in 2 cases of renal avian tuberculosis suggested benign septicemia with normal morning temperature and an evening rise (to 38.8° C.). The temperature in these 2 cases was uninfluenced by antipyretics; though the disease had lasted two years, the general condition of the patients was good. The local signs were not marked. Both of these patients who reacted only to avian tuberculin were treated with this substance and have remained free from symptoms for a year. The infection may result from eating the eggs of tuberculous hens, as the eggs may contain large numbers of tubercle bacilli. In experimentally infected eggs, soft boiled, the tubercle bacilli were uninjured; from two hard boiled eggs, viable bacilli were recovered.

Lymphocytosis in Chronic Polyarthritis.—F. GUDZENT (*Deutsch med. Woch.*, 1913, xxxix, 887) has made a careful study of the blood picture in 100 cases of chronic polyarthritis. The red cells and hemoglobin showed no noteworthy alterations. The leukocytes were normal in total number. Differential count showed a lymphocytosis in a majority of the cases. It amounted to 25 to 30 per cent. in 19 cases; 30 to 40 per cent. in 42 cases; 40 to 50 per cent. in 24 cases; 50 per cent. in 8 cases. In 9 cases the blood picture was normal. The lymphocytosis was present regardless of the stage of the disease. In view of the uncertainty of the etiology of this symptom complex, it is impossible to speculate as to the cause of the change in the leukocytic formula, but the association of increase in lymphocytes in chronic polyarthritis must be borne in mind when lymphocytosis is discovered.

SURGERY

UNDER THE CHARGE OF

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Three Cases with Large Calculi Which were Absolutely Latent.—PILLET (*Jour. D'Urolog.*, 1913, iii, 763) reports three very interesting cases with large renal calculi, all having an absolutely latent course. The first patient, aged thirty-six years, had had urinary treatment for several months and both ureters had been explored. A radiograph showed multiple large renal calculi, but the patient refused operation. The second patient, aged thirty-five years, had suffered since 1910 from burning urination. Each evening on returning from work, his urine was red and turbid, and slightly purulent. He urinated about every three hours, day and night. The radiograph revealed a large, coral-formed stone, 11 cm. long and 6 cm. wide, with prolongations into the calyces. The kidney was absolutely painless, because completely destroyed. The third patient, aged forty-three years, was operated on in 1909 by Pillet, for three calculi of the left kidney. This operation was followed by the expulsion of two small ureteral calculi after ureteral catheterization. In this case a friction sound had been obtained, by the use of the ureteral catheter, during stethoscopic auscultation of the abdomen. This patient, at the present time, presents in his opposite kidney, three calculi, clearly visible in the radiograph. One calculus is of the size of a hen's egg. Each of the other two are about as large as a hazel nut. The patient refuses to be operated on. A voluminous pyonephrosis has been developing for some years. It extends from the thoracic border to the pubis in the median line. One of the calculi can be felt distinctly under the skin by simple palpation. The patient does not suffer and having refused operation up to the present time, Pillet considers that it is no contra-indicated because of the degree of cachexia present.

Abscess of the Liver at the Haiphong Hospital.—SAMBRUC (*Archiv. gén. d. Chir.*, 1913, vii, 641) reports a study of 100 cases of suppurative hepatitis, collected from the Haiphong Hospital, during a period of thirteen years, with particular reference to their interesting clinical features. Abscess of the liver at Tonkin, is nearly always of dysenteric origin. The dysentery, however, is often unrecognized, either because it passes unperceived or it is in an abnormal form (intestinal amebiasis in diarrhetic form). The most frequent site of the abscess is in the

antero-superior portion of the right lobe (corresponding to the seventh, eighth, and ninth intercostal spaces, between the mammary and mid-axillary lines). It is four times less frequent in the left lobe. Those of the quadrate and spigelian lobes are very rare and never isolated. Multiple abscesses were observed in the proportion of 40 per cent. In 15 per cent. they were located, at least partially, along the inferior surface of the organ. Migration into neighboring organs, are usually, followed by death, unless the abscess is evacuated by vomiting, which is followed by cure in 50 per cent. of the cases. Spontaneous evacuation into the intestine, is fatal in 75 per cent. of the cases. The diagnosis of hepatic abscess is often very difficult. Some of the cases are atypical, simulating a thoracic lesion (pleurisy, tuberculosis), and abdominal lesion (appendicitis), or it evolves like a general infection (typhoid fever). There is no pathognomonic sign. The more characteristic symptoms may be missing, such as the hepatic pain and enlargement. The frequent existence of congestion of the liver, in the evolution of a dysentery, makes the errors in diagnosis much more frequent. One should suspect an abscess of the liver in all patients presenting a high afternoon temperature, of uncertain origin. Exploratory puncture alone, an inoffensive but often efficacious operation, can confirm the diagnosis. The diagnosis of multiple abscesses, is impossible to establish *a priori*. It is only by the evolution of the disease, after a first operation, that one can justly suspect the existence of other foci. In cases of probable abscess of the inferior portion of the liver, exploratory laparotomy is a logical operation. Juxta-phrenic abscesses are often unrecognized, because the exploratory punctures are made too low. The prognosis is severe, because of the extreme frequency of multiple abscesses. Among the postoperative complications, there is one that is often overlooked, the pleural effusion which, even when only small, is likely to cause death.

Histological Examination of the Gastric Mucosa in Gastric Ulcer and Carcinoma.—HEYROVSKY (*Deut. Zschr. f. Chir.*, 1913, cxxii, 359) says that the advance of modern pathological histology, has been due largely to the knowledge that only tissues preserved and fixed when living, give the true picture of the cell changes produced by disease. The gastric mucosa was removed with the lesion in a series of operations for gastric and duodenal ulcers and carcinomas, was fixed while in the living state, and was examined, histologically, with the following results: The material was obtained from 120 cases; of which 70 were cases of gastric ulcer, 7 duodenal ulcers, 15 carcinomas of ulcer origin, and 28 carcinomas without ulcer origin. A severe gastritis was found in 51.5 per cent. of the gastric ulcer cases, 42.9 per cent. of the duodenal ulcers, 66.6 per cent. of the ulcer carcinomas and 78.5 per cent. of the carcinomas without ulcer origin. The pathological changes in the mucus membrane, in all the above mentioned diseases, were almost the same and differed only gradually. In the cases of gastric ulcer associated with gastritis, no constant cause for the gastritis could be demonstrated. It was dependent in many cases on the duration of the gastric ulcer or the gastric stagnation. No unity could be shown between the histological picture of the fundus mucous membrane and the behavior of the gastric secretion. No characteristic changes could

be found in the fundus glands to account for the hypersecretion and hyperacidity. In the gastric ulcer cases, there were found frequent erosions of the gastric mucous membrane, which possibly play a role in the origin of the gastric ulcers. The ulcer patients who had, in addition, gastritis, after gastro-enterostomy, suffered more frequently from stomach troubles, than the patients with ulcer without gastritis. The histological examination of the gastric mucous membrane removed at operation, has great practical value with relation to the prognosis and the subsequent dietetic therapy.

A Contribution to the Functional Diagnosis of Gastric Disease by Means of Sahli's Method.—ZNOJEMSKY (*Deut. Zschr. f. Chir.*, 1913, cxxii, 393) calls attention to the fact that what we need most in connection with malignant disease of the stomach, is not improvement in technique, but the possibility of making an early diagnosis. He employed Sahli's method, with and without a modification of the test meal, in 700 cases and reports a series in which operation was performed. From his studies he concludes that a considerable diminution of the motility, secretion and acidity, and positive lactic acid, speak for carcinoma at the pylorus. Normal motility, diminished secretion and acidity, and positive lactic acid findings, speak for gastric carcinoma. Diminished motility, somewhat diminished secretion and acidity (lactic acid negative), speak for carcinoma at the pylorus on the base of an ulcer. Normal motility, somewhat diminished secretion and acidity (lactic acid negative), speak for gastric carcinoma on the base of an ulcer. Diminished motility, normal or diminished secretion, and hyperacidity, speak for pyloric ulcer. Normal motility, normal or diminished secretion, and hyperacidity, speak for gastric ulcer. Diminished motility, normal secretion and normal acidity, speak for gastroptosis. Normal or diminished motility, hypersecretion, almost normal acidity, speak for duodenal ulcer or ulcer behind the pylorus. Diminished motility, secretion and acidity, are usually a typical finding in cholelithiasis and Ren Migrants. Changing behavior of the secretion and acidity (now increased and now decreased), speak very often for pyloric spasm.

Radium in the Treatment of Malignant Disease.—KNOX (*Brit. Med. Journ.*, December 7, 1913, 1196), who is director of the electro-therapeutic department of the Cancer Hospital, Brompton, England, says that in all cases of early cancer the operative method is undoubtedly the best; it is quicker, safer, and offers the best prospect of cure. Radium is a useful adjunct to the treatment of all cases, first as a prophylactic after operation and, failing operation, the next best method we possess. It must, however, be stated that x-rays are in selected cases quite as useful as radium. In patients who refuse operation, or are for other reasons not suitable for operation, radium is a useful remedy. In inoperable cases radium may help to render the case operable; and failing that is undoubtedly useful as a palliative measure.

THERAPEUTICS

UNDER THE CHARGE OF

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Clinical Effects of "Natural" and "Synthetic" Sodium Salicylate.—HEWLETT (*Jour. Amer. Med. Assoc.*, 1913, lxi, 319) in an endeavor to ascertain the merits of the claim that the sodium salicylate prepared from natural oils is inferior as a therapeutic agent to the sodium salicylate prepared by synthetic methods, obtained data by the coöperation of a number of clinicians of recognized standing. They were asked to use and to note the effects of test powders of sodium salicylate without knowing the sources, natural or synthetic, of the individual powders. The result of the coöperative investigation as to the relative therapeutic value of sodium salicylate derived from natural sources and of sodium salicylate prepared by synthetic methods shows no essential differences between the two. This was demonstrated not only by the opinions of those investigators who attempted to classify the effects of their powders but also by a study of all the reports submitted. The slight variations in one direction or the other as shown by the figures are such as one expects in any set of statistics. Indeed, the statistical variations in these figures are surprisingly small. Allowing, therefore, for statistical error, one must conclude that natural and synthetic sodium salicylate are indistinguishable so far as their therapeutic and toxic effects on patients are concerned.

The Therapeutic Use of Benzol.—KIRALYFI (*Wien. klin. Woch.*, 1913, xxvi, 1062) writes from the clinic of Koranyi, who was the first to recommend benzol for the treatment of leukemia. Kiralyfi warns that in the future greater caution is necessary with regard to the dosage of benzol. He believes that it is advisable to discontinue the remedy as soon as the number of the leukocytes begins to decline. In any case the administration of benzol should be immediately stopped when the leukocyte count has reached 25,000 or 20,000. This precaution is necessary because the diminution of the leukocytes continues for some time after the withdrawal of the remedy. Kiralyfi quotes Neumann who reported a case where the continued use of benzol seemed to cause a rapid diminution of the leukocytes to as low as 200 per cubic millimeter associated with severe and uncontrollable epistaxis, the patient dying thirty-nine days after discontinuing the benzol treatment. Kiralyfi has had a similar case in which the remedy at first seemed to have a specific action against the disease, the patient feeling entirely well and the blood picture remarkably improved. The benzol treatment was discontinued but the leukocytes continued to diminish until the count was 2800. Severe epistaxis then occurred and lasted for seven days. Various local and general measures were

of little avail in controlling the hemorrhage, and finally the patient died twenty-two days after the withdrawal of the remedy. The leukocytes then were 460 per e.e., no myelocytes were found and only 3 per cent. of myeloblasts. This case had been regarded as a brilliant example of the curative action of the benzol treatment but Kiralyfi considers that the continued action of the benzol was responsible for the uncontrollable hemorrhage and final fatal result. Kiralyfi says that the benzol treatment has been tried in other affections than leukemia, mentioning various enlargements of the lymph nodes without increase of the leukocytes, the pseudoleukemias, and also polycythemia. Benzol seems to have the same effect in reducing enlarged lymph nodes as Röntgen-ray treatment, but the improvement is only temporary. Kiralyfi says that in true pseudoleukemia benzol has a marked and almost certain action upon the disease. He does not believe that nephritis is aggravated by benzol therapy, but, often, according to his experience, is definitely benefited.

The Vaccine Treatment of Typhoid Fever.—WALTERS (*Med. Record*, 1913, lxxxiv, 518) reports a total of 158 cases of typhoid treated by vaccines. These cases were in all stages of the disease and in the entire number there have been 17 deaths, a percentage mortality of 11. Among these fatal cases, Walters says there were 8 cases where for one reason or another but one dose of vaccine was given, and that when the patients were moribund or *in extremis*. Excluding these 8 cases and 2 others that died of complicating diseases, there has been a total of 7 deaths in the remaining 148 cases, or a percentage mortality of 4.7 among those where the treatment may be said to have had a fair trial. During this time a parallel series of 100 cases not receiving vaccines has been observed, and here there have been 13 deaths or a mortality of 13 per cent. Walters collected a series of 1120 cases treated by different observers and believes that results thus obtained are more suitable for statistical purposes. In this series of 1120 cases, there was a total of 67 deaths. Excluding certain of the deaths upon grounds similar to his own series of cases, the mortality percentage in the entire series was 5. The percentage of relapses was also much reduced, being 6 per cent. as compared with the 15, 20, or 25 per cent. usually reported. From his personal experiences and the statistics of others, Walters summarizes certain things he has learned, and believes that certain measures he has used can be improved upon. He says that the best results have been attained by preparing vaccine from an old, non-virulent culture which has been subcultured for years in connection with the Widal tests. A new culture is made from this and incubated for twelve hours. In comparing his dose with that of others, it seems probable that his may be increased to 100,000,000, 200,000,000, or possibly 500,000,000. An early diagnosis is most important; this can often be first made by blood culture, days before the Widal reaction appears. The vaccines, when properly used by an immunizator will not harm in any stage of the disease, or in a relapse; but the earlier they are used, the greater the prospect of benefit. A safe rule to remember is that the more severe the case, the smaller should be the dose. The interval between doses is variable. A dose or two after the temperature has reached normal will render relapses less frequent.

PEDIATRICS

UNDER THE CHARGE OF

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Vulvovaginitis in Young Children.—NATHANIEL BARNETT (*Archiv. Pediatrics*, 1913, xxx, 650) gives a report of studies in a special clinic for this class of cases. The spread of the disease is favored in hospitals where individual cases are not isolated and in schools where children use a common toilet. Crowding of children and adults in small homes of the poor also favors its spread. Out of 50 cases studied, 14 contracted the disease from the mother or sister who had a vaginal discharge, and with whom the patient slept. Chronicity and resistance to treatment are characteristic of this condition. The average duration was eight and a half months, the largest record of persistence of the disease was six years. The external appearance of the hymen may be normal but pus is usually found behind it. The cervix is deeply congested and pus exudes from the orifice. Superficial ulcerations are often seen on the cervical lips. A urethral speculum is used to explore the vagina. The complications in this series were arthritis of shoulder and wrist, chronic general peritonitis, pelvic peritonitis, and painful heel. The treatment consisted of irrigations of potassium permanganate 1 to 1000; bichloride of mercury 1 to 4000; Lugol's solution, 1 to 500; instillations of silver nitrate 0.25 per cent. and argyrol, 10 per cent. Vaccines which improved the complications, such as arthritis, had absolutely no effect on the local condition. After thoroughly testing various forms of treatment the following was adopted as the best. Daily vaginal douche of potassium permanganate solution 1 to 10,000; small daily doses of urotropin; use of the Kelly endoscope three times a week with direct application to the cervix and vaginal walls of Lugol's solution. Cases are considered cured if smears taken weekly are negative for three consecutive weeks. Out of 26 completed cases 7 were cured at the end of six months by irrigation alone. Out of 7 cases not responding to irrigations, 5 were cured in one month with the endoscope. Direct applications must be made to the deep point of infection. Cures can be obtained in a short time by treating the cervix with strong solutions. Prophylaxis is difficult. Sleeping alone, wearing a vulvar pad, individual sets of clothing, and keeping the hands away from the genitals are important points.

Radiographic Studies of the Gastro-intestinal Tract.—HENRY DWIGHT CHAFLIN (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1419) reports his findings in a number of tests to determine the mobility and motility of the gastro-intestinal tract, by the rapidity with which a suspension of barium sulphate could travel from the stomach to the cecum and thence through the large intestine to the outlet of the body. The radiographs show the stomach almost free of barium within two hours after ingestion of the barium and most of the suspension in the small intestine.

In three hours and ten minutes the greater part of the barium was in the cecum, ascending colon, and hepatic flexure. In six hours the transverse colon also was filled up to the splenic flexure. In seven hours the rectum was well distended with barium and a considerable amount remained in the descending colon. In one radiograph a noticeable amount of barium is seen in the small intestine within twenty minutes of its being placed in the stomach. These tests were made on children of seven and eight months of age. Another series of cases was studied after a clysm of barium had been given to determine the form and location of the sigmoid flexure, distensibility of the colon, and patency of the ileocecal valve. The pictures were begun right after the injection. A great variability was observed in the mobility of the hepatic and splenic flexures and the transverse colon. Injected substances getting past the sigmoid flexure reach the cecum very quickly. In one case the ileocecal valve was patent. The sigmoid flexure varied remarkably in form and situation. It seems to occupy greater space than has been supposed and may be twisted and doubled up in all directions during life and may occasionally reach as high as the transverse colon. This bears out the claim of Boas and Nothnagel that it is rarely if ever possible to pass a tube through this structure.

Relapsing Pneumonia in Children.—R. R. ARMSTRONG (*Brit. Jour. Child. Dis.*, 1913, x, 444) gives the division of acute pneumonia in children into lobar pneumonia which is least common; lobular which is most common, and that condition associated with suffocative or acute capillary bronchitis with peribronchial pneumonia. Delayed resolution occurs most frequently in the lobular type. Relapsing pneumonia generally gives well-defined clinical signs and Armstrong describes 4 cases which demonstrate this. These 4 cases each lasted thirteen weeks and began with fever and cough. The original lesion in the lung cleared up in these cases in five to seven days with a drop in temperature to normal or almost normal. Then, in from one to several days, the temperature would again rise and the signs of dyspnea, etc., again appear. On examination a fresh area or lobule was found to be affected. These relapses occurred as often as eight times during the course of the disease. Usually the upper portions of the lung were secondarily affected, even the apices; new areas of consolidation appearing with each relapse. In the earlier relapses the bouts of pyrexia were prolonged and the intervals of normal temperature short. As illness progresses, however, the bouts of pyrexia are short, the fever never rises very high and fresh areas of infiltration, if present, are difficult to define. The pneumococcus was obtained in pure culture from two of the cases, the other cases were undoubtedly due also to this infection. Vaccine treatment showed no definite results. Strumous changes noted in some of these cases are possibly due to pneumonic toxins and a diagnosis of tuberculosis should not be made in long-continued pneumonias without examination and absolute proof clinically. The similarity between some children with chronic pneumonia and cretins suggests that thyroid extract may at times assist in promoting resistance to infection from pneumococci.

OBSTETRICS

UNDER THE CHARGE OF

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Bacteriological Examination in Fever Occurring During Labor.—SACHS (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, lxx, No. 1) has studied the occurrence of fever during labor from the standpoint of bacteriology. He finds that where hemolytic streptococci are present in the birth canal they may cause fever during labor, whether in pure culture or not. The temperature may rise rapidly, and apparently without other cause. Other sorts of bacteria produce fever after much longer labor. In these cases other complications, such as placenta prævia, the use of the tampon, or the presence of predisposing blood clot, are of importance. The so-called streptococcus viridans seems to have little effect in producing fever during labor. The *Bacillus coli communis* produces fever rapidly, but, when in pure culture and in labors not unduly protracted, they produce no dangerous infection. Staphylococci are of very little importance in the production of fever during labor. In rare cases they become so virulent as to produce an effect. In cases that are not in the hospital, and in emergency births, such as those sometimes occurring in railway stations, in shops, or upon the street, if repeated examinations were made, bacteria which ordinarily are not pathogenic, may produce fever during labor. Thus, in one case the *Streptococcus viridans* was present in a case complicated by transverse position and rupture of the uterus. In another case, infection with the colon bacillus developed in transverse position, which made necessary the amputation of the fetal arm.

As regards the character of the fever and the condition of the pulse, streptococcus infection produces a rapid pulse—usually to 100 and often above. In other varieties of infection the pulse often remains below 100. In general, it may be said that with a temperature of 103.5° to 104° , and pulse above 100, that streptococcus infection is undoubtedly present, and with a low pulse and temperature the infection is from some other less virulent bacillus. As regards infection during labor, and its result in the puerperal period, the duration of labor accompanied by infection does not have great influence, nor does the causal element in producing fever during labor enable one to judge concerning what will happen in the puerperal period. Should labor be greatly prolonged, with fever, the puerperal period will undoubtedly be complicated. The occurrence of decomposition with foul lochia and with chills, does not necessarily indicate severe complications after birth. When we consider the variety of bacteria which produce fever during labor and its influence upon the puerperal period, we find that the morbidity during the puerperal period in streptococcus infection of the hemolytic variety, is three times as great as with any other. Where the puerperal period is greatly complicated by fever and other varieties

of organisms are present, there has been some other element to account for the complication. The presence of a pure culture is of significance in streptococci only. There is, however, a great influence exerted upon the puerperal period in the method of delivery. The more extensive and prolonged the interference, the greater is the development of fever and other complications in the puerperal period. The more virulent the infection during labor, the more imperative is it to avoid wounding the patient's tissues during labor. Spontaneous labor is to be secured, if possible, in this case.

Labor Complicated by a Gauze Pad Left in Douglas' Pouch.—DOLERIS (*Bull. de la Soc. d'Obstét. de Paris*, July, 1912) reports the case of a patient upon whom section was performed following pelvic inflammation. Pregnancy afterward developed, and, upon examination, the cervix was high up behind the symphysis and the vagina blocked with a bulky mass which filled Douglas' pouch. This resembled in feeling a universally adherent dermoid cyst. Labor came on without progress, and delivery was effected by Cesarean section. After the uterus had been closed, a deposit of organized lymph was found behind the uterus covering the pelvic cavity, and resembling a fold of peritoneum. When this was carefully opened, thick pus exuded freely. This membrane was carefully incised and a mass lying beneath it removed, which proved to be a gauze pad that had been in the pelvis over a year and a half. In view of the infection present, hysterectomy was performed, drainage inserted, and serum was administered with stimulants. During the second day there was distention, with urticaria, and later the right parotid gland inflamed, but this complication disappeared within twenty-four hours. The patient gradually recovered.

Arterio-venous Transfusion in Puerperal Hemorrhage.—OUR (*Annal. d. Gin. et l'Obstet.*, November, 1912) has frequently used intravenous saline transfusion in postpartum hemorrhage, and usually with satisfactory results. In the case of a young multipara, pregnancy was complicated by infection of the right kidney. Just before term the patient had hemorrhage, and, on examination, the membranes were found ruptured, the head engaged, but the placenta separating, with internal hemorrhage. The patient was delivered with difficulty with very copious bleeding, as the placenta had become completely detached. Other methods failing, and the patient becoming unconscious, it was determined to try arterio-venous transfusion. Accordingly, the husband's right radial artery was anastomosed with the patient's right median cephalic vein. Local anesthesia was employed for the husband. The transfusion was continued for nearly an hour, with evident improvement in the wife and without a sign of syncope on the part of the husband. The anastomosed vein and artery were resected a little above the line of suture, and no contraction or coagulation could be detected. The patient's improvement was immediate, and her convalescence was prolonged by the pyelonephritis. She finally, however, made a complete recovery, which is ascribed to the direct transfusion.

GYNECOLOGY

UNDER THE CHARGE OF

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Conservative Surgery in Genital Tuberculosis.—PATEK AND OLIVIER (*Rev. de Gyn.* 1913, xxi, 25), report the results of the recent examination of 33 patients upon whom some form of conservative operation had been performed since 1900 for tuberculosis of the internal genitalia. They used the vaginal route in only four instances, and think it should be discarded altogether, as it does not give the clear view of the affected area which is essential to the proper performance of any type of conservative operation. Simple laparotomy, without the removal of anything, as has been advocated by some authors, they also condemn, believing that no good is accomplished by such operations, except possibly in a very few far advanced cases, where anything more radical is out of the question at the time. In such instances, a simple laparotomy may occasionally lead to a temporary amelioration of conditions, and thus permit of a second, more radical procedure. Operations in which the uterus is allowed to remain, although both tubes and ovaries are removed, are likewise considered unjustifiable; such a uterus is useless, and although it may appear perfectly healthy, it may subsequently become tuberculous and require removal, as in one of Patek and Olivier's series. In rare instances, however, the uterus may be so densely surrounded by tuberculous exudate that to remove it would add tremendously to the shock of the operation; in these cases, they consider it justifiable to leave the uterus, even if both adnexa have been removed. Most of Patek and Olivier's cases in which true conservatism was practiced have done exceedingly well, and have regained excellent health, though a few continue to suffer from abdominal pains, and on examination are found to have a tender pelvic exudate. One woman, from whom everything was removed except one ovary, underwent all the symptoms of the artificial menopause. In only one instance did pregnancy subsequently occur; the sterilizing effect of the tuberculous process is so great that such cases must always remain the exception, so that the possibility of preserving this function does not carry much weight in determining in any given case the type of operation. In questioning a large number of women upon whom the *radical* operation had been performed for genital tuberculosis, one of the authors has brought out the interesting point that such patients complain very little of the symptoms commonly associated with the artificial menopause, this probably being due to a slow reduction which has taken place in the ovarian activity as a result of the tuberculous infection, thus gradually accustoming the organism, as it were, to its absence. In view of this fact, and of the slight chance in most instances of a subsequent pregnancy, Patek and Olivier believe that conservatism in dealing with genital

tuberculosis is indicated more on sentimental than practical grounds; they do consider it justifiable in young women, however, where the ovaries themselves are not found distinctly infected; where such is the case, only the truly *radical* operation (removal of uterus with both tubes and ovaries) can be depended upon to cure.

Tuberculous Pyosalpinx Perforated into the Bladder.—ISRAEL (*Deutsch. med. Woch.*, 1913, xxxix, 2295) reports a most unusual case of genito-urinary tuberculosis, occurring in a young girl, and presenting several features of interest from both the diagnostic and therapeutic standpoint. When the patient first consulted him, at the age of twenty-two years, she complained of failing health for the previous years, with increasing dysuria, night sweats, and feverish attacks. The urine was cloudy, contained pus, and on one examination tubercle bacilli, though on several subsequent examinations these could not be found. Cystoscopic examination showed a much inflamed bladder, with a tuberculous ulcer on the right side, and urine from each kidney, obtained by ureteral catheterization, produced tuberculosis in all inoculated animals; the same results were obtained upon a second examination. The case was therefore diagnosed as one of bilateral renal tuberculosis, unsuitable for operation, and sanatorium treatment advised. After eleven months of this the patient returned having gained 38 pounds, and presenting the appearance of perfect health. Cystoscopic examination again showed much inflammation, but no ulcer; palpation of both kidneys was absolutely negative. Israel's suspicions were now aroused as to the correctness of the former diagnosis, and a careful bimanual examination was made under ether, revealing an indefinite tumor mass in the neighborhood of the uterus, reaching to above the symphysis. Following this examination there was an intense febrile reaction lasting several days. A second ureteral catheterization was now undertaken with the greatest precautions to prevent any bladder urine from flowing out through the catheters; the urine obtained in this manner gave absolutely negative results in all injected animals, whereas that from the bladder uniformly caused death from tuberculosis. The true nature of the case was now clear; the kidneys were healthy, and the urine obtained from them at the first two ureteral catheterizations had been mixed with that from the infected bladder during the passage through it of the catheters, and had thus given the positive guinea-pig reactions. The mass felt was evidently a tuberculous focus communicating with the bladder, and intermittently discharging into it. A laparotomy confirmed this opinion; a tuberculous pyosalpinx was with great difficulty shelled out of a dense mass of pelvic adhesions, a distinct band, containing a lumen, being demonstrable between it and the bladder wall. Following the operation the urine gradually cleared up, and all symptoms disappeared rapidly, but tubercle bacilli remained for six months before entirely disappearing. The abdominal wound, however, gave much trouble, numerous fistulous tracts being formed, but after about seven months healing finally took place. Two years after operation the patient reports excellent health.

OTOLOGY

 UNDER THE CHARGE OF

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Local Anesthesia of the Drum-head.—BLEGVAD (*Deutsch. med. Woch.*, xxviii, 1912) says that under normal conditions the drum-head is practically impermeable, because of the superimposed layers of pavement epithelium forming its outer coat, so that the admission of fluids from without to the deeper tissues is possible only through some solution of continuity of the dermoid coat. This fact has been availed of by Gray and Bouerius with good results, a removal of a limited area of the resistant tissues, either by incision or by erosion before application of the anesthetic solution having sufficed to effect a deadening of sensibility throughout the drum-head sufficient to permit of paracentesis, of multiple incisions, the removal of small polypi and other circumscribed operations, with only slight discomfort. To the character of the anesthetic, in both instances, Blegvad takes exception on account of their toxic properties, that of Gray containing analine oil to the extent of from 50 to 70 per cent., and of Bouerius phenol in addition to cocaine, and recommends, as a substitute, cocaine and salicylic acid in equal parts in double the quantity of absolute alcohol with the addition of a 1 per cent. adrenalin solution.

Angiosclerotic Otagia.—Within a period of ten years STEIN (*Wien. klin. Woch.*, 1912, xxvi) had observed 246 cases diagnosticated as arteriosclerosis upon the basis of both the general and the aural examinations. Of this number 37 or 15 per cent. complained of discomfort or pain in the region of the ears, but so far as a demonstrable local cause for pain was concerned, the aural examination was, in all these cases, negative. The pain was usually directly localizable, in the depth of the ear, not infrequently in the external auditory canal, and sometimes in the mastoid region and the sensations, which were usually monaural, rarely binaural, were described as pressure, stretch-pricking or resembling a cramp, they were either continuous, with variations in intensity, or intermittent and were referred, by Stein, as the result of a series of observations of the general as well as the local manifestations, to arteriosclerotic changes in the bloodvessels distributed to the ear which, by decreasing or interrupting the blood supply evoked the painful sensations familiar in other regions. Good results were attained by the administration of diuretin in 0.5 gm doses from three to five times daily, continued for several weeks, in more than one-half of the cases so treated the pain was decreased and finally disappeared.

Effect of Auditory Stimuli upon the Cerebral Circulation.—In the case of a young man, aged seventeen years, who, as the result of operation following an extensive fracture of the skull, had a cranial

opening in the frontal temporal region 13 by 8 cm. in area, CASTELLAN (*Archiv. International*, 1913, xxxv, 1) had an opportunity to repeat the observations of Dogiel and, in a measure, confirm them. Over the greater part of the bony defective space the skin of the scalp was in contact with the dura and partly adherent, rendering the diffused pulsation of the brain, synchronous with the radial pulse, both tangible and visible. In the right ear the middle ear was apparently normal, but the hearing was entirely wanting while the left ear heard normally. By attachment to the skin of the surgically created cranial foramen of a manometric capsule with a kymograph it was possible to still further observe, and to record, the cerebral pulsation in response to the acoustic stimulation of the left ear by means of tuning-fork tones applied close to the auricle. In response to the deeper-toned forks C2, C1, and C, the cerebral pulse increased in frequency with a slight decrease in the primary and an increase in the secondary impulse, indicating a decrease in arterial tension. Tones of medium and high-pitched forks were accompanied by a slight, but definite diminution in frequency, a marked elevation of the recorded curve, consonant with the increased blood pressure, and either a disappearance, or a marked decrease, of the secondary impulse.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Changes Occurring in the Voluntary Muscles in General Diseases.
—JEWESBURY and TOPLEY (*Jour. Path. and Bact.*, 1913, xvii, No. 4) have conducted some interesting experiments dealing with the state of the muscles in certain so-called general diseases. In wasting diseases they find various degrees and kinds of histological change which do not seem closely related to the degree of wasting present, but which seem rather to be the result of intercurrent inflammation or toxemia. In acute general diseases, such as pneumonia, septicemia, diphtheria, eclampsia, etc., the changes are usually of the nature of hyaline or granular modification of the muscle cell and occasional fatty degeneration. In disorders of carbohydrate metabolism there is a very marked increase in the amount of interstitial fat. They found a small collection of fat droplets in the neighborhood of the nuclei frequently in advanced life, rarely in children, and very rarely in animals. The pathological significance of this fat Jewesbury and Topley were unable to determine. The most interesting point of their observations is that the incidence of fatty degeneration has been much over-stated; nevertheless, they found it very marked in diphtheria and phosphorus

poisoning, in infective purpura, and in severe anemia. Glycogen was sought for in a large variety of diseases, but it was found in considerable amount only in diabetes. Amyloid change was not found in the series, although 12 cases were examined whose nature would render the presence of amyloid in the muscle a possibility.

Blood Platelets in Blood Repair.—LE SOURD and PAGNIEZ (*Jour. de Phys. et Path. Gén.*, 1912, xiv, No. 6) have made experiments with a view to determining the part played by the platelets in repair of blood loss, and find that they can alter the platelet content without necessarily changing the red corpuscle content of the blood. The outburst of hematoblasts following upon an excessive bleeding can be prevented without at the same time preventing the repair of the blood loss; so that these two processes which appear to be very intimately connected can actually be dissociated. That the platelets and red blood cells are not intimately associated, is also seen in cases of purpura hemorrhagica, where the number of platelets may sink very greatly, or may even sink to zero, while the red blood cells preserve their normal number. Nevertheless, in the majority of cases, numerical variations of the platelets do run somewhat parallel to that of the red cells, and the determination of a rapidly increasing platelet count determines a favorable degree of activity in the blood-forming organs; on the contrary, the progressive and permanent lowering of the platelet count coinciding as it does with the lowering of the red corpuscle count in pernicious anemia, is a further indication of the inactivity of blood-forming organs. Le Sourd and Pagniez consider that the previous statements of Achard and Aynoud were correct, when they considered the platelets as numerically variable, independent of the other elements of the blood.

An Improved Method for the Histological Study of the Arteries.—MACCORDIC (*Jour. Path. and Bact.*, 1913, xvii, No. 4) has devised an extremely useful method of studying arteriosclerotic and other arteries, without the preparation suffering from the contraction which usually occurs post mortem, and which is responsible for a histological picture actually much different from that obtained in an artery whose natural state is preserved after death. MacCordick has succeeded in permanently relaxing the artery by subjection to a solution of ammonium sulphocyanide. After removing a piece of artery from the body it is immersed in 20 per cent. solution of the above substance, then washed in normal saline, and to each end of the artery a small glass cannula with rubber tubing is attached. While remaining in saline solution, air is pumped in, and the presence of small branches is noticed by the escape of air bubbles; such branches may be readily ligated. The artery is next attached by means of these tubes to a pressure apparatus with a manometer, and Zenker's solution or 10 per cent. formalin is pumped into the artery, which meantime is immersed in a similar solution. By additional force, the tubes being clamped, the pressure of the solution inside the artery is raised to 150 mm. of mercury, although for normal arteries a pressure of 100 mm. answers the purpose. This pressure is kept up during twenty-four hours, at the end of which time the artery is permanently fixed. MacCordick's

diagrams indicate how perfectly the *intra vitam* state of the artery is preserved. Subsequent to fixation the tissues are treated in the usual way. While the suggestion for this piece of work arose in MacWilliams' publications, nevertheless the application of this usefully modified procedure to diseased arteries, seems to rest with MacCordiek.

Factors in the Formation of Metastatic Tumors.—TYZZER (*Jour. med. Research*, July, 1913, xxviii, No. 2, 309) experimented upon mice in which tumor metastases were developing, and draws the practical conclusion that manipulation of a tumor, even in its early stages, is apt to cause metastasis, and that handling and massage are more likely to cause metastases than is section of the primary mass: the deduction for the clinician is a simple one. Operation which includes section of the primary tumor does not increase the liability to secondary growth; secondaries grow more rapidly, however, after removal of a large mass of tumor tissue elsewhere (the so-called *athrepsia* of Ehrlich), as well as under improved physical conditions of the body. In the mice operated upon, Tyzzer had, by long observation, noted accurately the time of appearance of secondary growths, and if removal of the primary tumor was undertaken just prior to this time, secondaries did not arise. The period called "premetastatic" exists rather on account of the absence of the conditions necessary for dissemination than on account of any resistance inherent in the body. Manipulation of the primary tumor shortens the duration of this premetastatic period.

The Pathological Anatomy of Paratyphoid Fever.—SALTYKOW (*Virchow's Arch.*, 1913, Band cxx) collected 22 cases of this affection from literature, of which 14 showed implication of the lymphoid tissue, ulceration being present in 9. Without being in any sense typical, the lesions of paratyphoid are very similar to those of typhoid. In the latter disease, it is interesting to note that PURJESZ and PERL (*Wien. klin. Woch.*, 1913, No. 40) found the characteristic bacilli, 4 times out of 7 patients, in the tongue-scrappings and upon the tonsils; in half of the *convalescent* patients examined, the bacilli were demonstrable at times varying from the fifth to the forty-seventh day after the active disease had subsided. The tongue gave positive results oftener than the tonsils.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.

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Wm Mitchell

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ORIGINAL ARTICLES

TUBERCULOSIS OF THE BREAST.

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THE original observations of Sir Astley Cooper (1829) undoubtedly placed the breast among organs subject to tuberculosis. It is rather remarkable, therefore, that Sir Astley's lucid description of the macroscopic features of "scrofulous swelling of the bosom" did not lead to a larger number of reported cases in the literature of the succeeding half century. Again, errors inherent to clinical observation preclude unreserved acceptance of all cases so reported before the advent of microscopic pathology. With perfection of the latter, and the consequent eviction of the infectious granulomas from the group of tumor diseases, Dubar was enabled, in 1881, to prove the breast as subject to tuberculosis on microscopic grounds. This report, although somewhat belated in comparison with the earlier microscopic recognition of other forms of surgical tuberculosis, marks the real beginning of our knowledge of its mammary form. Indeed, little has been added to Dubar's original description.

Subsequent writers have discussed the condition principally from the standpoint of primary and secondary involvement. This is a question that must fail of absolute solution in any given case, since postmortem examination is the final word in its establishment. We must, however, classify all proved cases of mammary tuberculosis as primary—the solitary tuberculosis of Geïssler—in which physical examination disproves the involvement of other organs. A positive tuberculin reaction after resection of a supposed primary

focus of the disease does not prove the presence of a hidden lesion, for, as Halsted has shown, these individuals react to the test as the result of bacillary products in the blood and not because of the presence of living organisms or their diseased tissue products.

The diagnosis of mammary tuberculosis can only be made with absolute certainty by means of bacteriological or pathological study. Chronic suppurative mastitis may pursue a clinical course to the formation of multiple fistulas that makes this condition undistinguishable from tuberculous mammæ. The same difficulty is experienced in the absence of suppuration and fistula formation in the differentiation of tuberculosis, gummas, neoplasms, and cystic conditions of the breast. For this reason we have excluded from our series of collected cases all those in which the diagnosis is unsupported by laboratory confirmation, however typical the clinical history and physical findings. The diagnosis then depends upon microscopic recognition of the anatomical tubercle, the presence of the tubercle bacillus in stained smears of pus from an abscess, or discharge from the nipple or sinus, in stained tissue sections, or depends upon cultural demonstration of the organism, and finally upon the development of the disease in susceptible animals after inoculation. The tuberculin reaction is probably of the same uncertain diagnostic value in the mammary as in other forms of tuberculosis, although it has never, so far as we have found, been used in this connection. In a certain proportion of cases in which the tissue reaction to the tubercle bacillus results in an atypical sclerosis, a type to which Scott has drawn attention, the diagnosis, in the absence of the bacilli in tissue sections, must be problematical. Ohnacker, in the year 1883, following Koch's announcement of his discovery of the *Bacillus tuberculosis*, reported 2 cases of mammary infection, the first in which the identity of the disease was made by animal inoculation. Additional case reports followed, often with insufficient study to fix, without question, their pathogenesis, until 1901, when Roux subjected the cases reported since Dubar's time to critical analysis. Roux accepted only 31 cases as authentic. This author reported 3 personally observed cases, in 2 of which the tubercle bacillus had been found. He added a third pathological type, the intraglandular cold abscess, to the confluent and nodular varieties first suggested by Velpeau and described in greater detail by Dubar. Since Roux's time the literature has been reviewed and cases reported, among others by Powers, 1894; Scudder, 1898; Bartsch, 1901; Anspach, 1904. Since the appearance of Anspach's paper, Scott, Schley, Geissler, Braendle, Fuller, and Powers have contributed excellent papers on the subject, but the time seemed opportune for a complete review of the cases reported since Anspach's studies in 1904.

As mentioned above we have disregarded all those cases unsupported by microscopic diagnosis. The cases are divided into

primary and secondary groups. We have accepted as primary only those cases in which the disease was confined to the breast and axillary nodes of the same side. It is, of course, probable that the disease in a number of instances primarily attacked the lymph nodes with secondary invasion of the breast. The histories of 5 personally observed cases are added to the list.

PRIMARY MAMMARY TUBERCULOSIS. The occurrence of primary tuberculosis of the breast is denied by many observers, including Klebs and Ribbert. It is evident that the cutaneous covering of the organ may become involved and constitute a local process in the same manner as lupus of other areas is produced, the pathogenesis of which was long since shown by Friedländer. Demme, Pluyette, Orthmann, and Kramer have reported cases of mammary tuberculosis in which the organism gained entrance to the tissues through abrasions of the skin and nipple. These observations refute the opinion of the writers quoted above, and more recently expressed by Spediacci, that all mammary tuberculosis is secondary. Babes has shown that the tubercle bacillus may gain entrance to the body thorough an apparently unbroken skin. That these organisms may pass through uninjured mucous membranes has been conclusively proved by Ravenel experimentally. The frequency of infantile mesenteric tuberculosis in the presence of an intact bowel wall is a familiar clinical support of Ravenel's views. Tuberculous infection *via* the lactiferous ducts incites a primary focus in the alveoli of the breast. This avenue of infection must, however, be extremely rare, and certainly one impossible to prove in the late stages when the interstitial tissues are invaded. Instances of ductal infection have been reported by Verneuil and Verchere. Primary involvement of the breast with tuberculosis by blood or lymph-vascular infection, presupposes the absence of the disease at the point of entry of the organisms. Blood dissemination is rare, and usually incites a rapid and generalized tubercular process. Primary mammary tuberculosis through blood-vascular infection means that the bacilli have gained entrance to the blood-stream directly, have not caused disease at the point of entry, and have localized themselves entirely to the breast tissues—a rather far-fetched hypothesis. The above applies equally to primary mammary tuberculosis through lymphatic infection.

SECONDARY MAMMARY TUBERCULOSIS. With the few exceptions of direct inoculation of the breast, through abraded surfaces of the nipples and skin and possibly through the milk ducts, all mammary tuberculosis is most likely a secondary manifestation of the disease. Most of the primary cases are so considered because the original focus is undemonstrable. In the great majority of cases the bacilli reach the breast through lymph channels, probably by retrograde embolic processes. The most important primary foci are located in the axillary, cervical, and retrosternal lymph nodes, and the adjacent

ribs, sternum, pleuræ, and lungs. The tubercle bacillus may perhaps reach the breast through lymphatic channels in the absence of lymph-node involvement. Analogy may be drawn from the involvement of cervical lymph nodes through tonsillar channels without any evidence of disease in the latter. We know that the urine and bile of tuberculous subjects may contain tubercle bacilli at times in the absence of renal or hepatic localization. Hirschberger produced tuberculosis in laboratory animals by inoculation with the milk of tuberculous cows, the udders of which were entirely free of disease.

Niepce observed a case of infantile infection in a child born of healthy parents, due to bacilli-laden milk from a wet-nurse. Rogers and Garnier report a case in which the milk was proved infectious by animal inoculation and the breast found normal at autopsy. No obviously tuberculous mother is of course allowed to nurse her infant, but we believe the restriction should be applied to all mothers who are suspected of harboring a tubercular process, however latent.

Every case of tubercular mastitis should be looked upon as harboring the disease after the removal of the involved breast, and should, therefore, be kept under strict regimen lest the disease remanifest itself. When the disease is limited to the upper outer quadrant of the breast and associated with enlarged nodes of the anterior pectoral subgroup of the axillary chain, in certain cases with a palpable band of neoformation joining the two foci, it is impossible to determine the primary area of disease. The breast in these instances is probably secondarily involved, but in the absence of a clear history indicative of this sequence of events we have not excluded these cases from the series of primary infections. Infection of the breast tissues from a contiguous focus by direct extension is of comparatively common occurrence. Two of our cases illustrate this feature of the disease. The history of one of these is as follows:

M. H., aged twenty-six years; single; stenographer. Admitted to the German Hospital April 20, 1912, complaining of a painful lump in the right breast. The patient first noticed the lump four months before admission. Her attention was drawn to the breast by pain on deep breathing at the site of the lump. The latter when first discovered was hard and tender, but later became soft and cystic.

Examination showed an encapsulated cystic tumor about the size of a hen's egg, in the lower inner quadrant of the right breast. The overlying skin was normal. General physical examination revealed nothing except a scar on the back at the site of a previous "gathering." A well-encapsulated cystic tumor was exposed after the plastic method of Warren. The sac, which was attached to the sixth rib, was excised and the rib carbolized. The wound was packed with gauze. The patient made an uneventful recovery.

In our second case the disease was of two years' standing. The mammary process was of the nodular type, although an area of softening was connected by a small sinus tract to the rib. There was no suggestion of an abscess in this case (shirt-stud abscess), said to occur in this type of the disease, owing to the resistant deep pectoral fascia.

Parsons reports a similar case in a young Italian laborer.

Invasion of the breast from a primary osteitis of the sternum is exceedingly rare. An instance of this type of infection is included in the series of Hardouin and Marquis. This patient was operated upon in 1890 for osteitis of the lower end of the sternum. Two years later a tumor appeared in the lower inner quadrant of the right breast. This was found at operation to be connected by a fibrous cord with the site of the primary focus. The diagnosis was not confirmed pathologically, so the case is not included in our series.

Gaudier and Peraire have reported a similar case.

Twenty-nine of our collected cases were looked upon as representative of the secondary type of the disease. The following table shows the site of additional foci of the disease in these cases.

	Cases.
Bilateral axillary lymph-node involvement	4
Pulmonary tuberculosis	4
Enlarged cervical lymph nodes	5
Tubercular osteitis of the ribs	3
Tubercular osteitis of the jaw and bones of the forearm	1
Axillary adenitis	5
Cold abscess of the forearm	1
Tuberculosis of the lower jaw and cervical nodes	1
Pleurisy	1
Tubercular hip	1
Tuberculosis of the finger and lungs	1
Entire axilla filled with a mass of tubercular lymph nodes	1
Tubercular knee	1
Total	29

A most interesting case is reported by Duvergey, in which the evidence of a retrograde lymph-vascular infection of the breast is almost irrefutable. The patient suffered a slight excoriation of one of the fingers of her left hand in September, 1910 while washing linens of tuberculous hospital patients. The wound suppurated for about two weeks and then healed completely. During the succeeding winter the patient noticed that she was steadily losing weight without any apparent cause. In April, 1911, she noticed a painful swelling in the left axilla. This increased in size, and in May it was incised, with evacuation of a large amount of serous and granular material. The wound did not heal. In July she felt pain in the left breast, and a swelling appeared above the nipple. This was opened and a large quantity of serogranular pus removed. Immediately two small abscesses appeared near the site of the incision.

These opened spontaneously and the three sinuses increased in size, and as a result of progressive ulceration, finally united. In the meantime another lump appeared in the subclavicular space and progressed to fistula formation. Other sinuses appeared from time to time and the axillary and upper mammary regions became united in one "vast ulceration." The apices of the lungs eventually became involved. Tubercle bacilli were found in the discharge from the sinuses.

Analogous cases are reported by Scott, Vignard and Pasquier, and Schmidt. This clear sequential order of events is lacking in the majority of cases, but it is probable that the bacilli reach the breast from the cervical lymph nodes in the same manner. In cases reported by Cignozzi, Bahuand, Scott, and Braendle the first manifestation of the disease appeared in the cervical lymph nodes. The fact that in these cases the axillary nodes escaped merely supports the well-known pathological fact that the lymphatic nodes may transmit infectious organisms without becoming involved in the disease process. It is impossible to chart the avenues of bacillary transmission from the lungs to the breast. The usual route is probably by way of the communicating trunks between the retrosternal chain and the breast. These branches follow the mammary branches of the internal mammary artery. Here again the process is a retrograde one. In cases reported by Hardouin and Marquis and Abraham and Khesin, in which there was antecedent joint tuberculosis, it would seem rational to look upon the bloodstream as the medium of dissemination. We may therefore consider the breast subject to primary tuberculosis as the result of infection through abrasion of the mammary skin or nipple, through the milk ducts, and rarely as a result of lymph- and blood-vascular infection.

Secondary mammary tuberculosis arises by direct extension from a contiguous area of infection or from blood- or lymph-vascular metastasis from a distant focus.

INCIDENCE OF MAMMARY TUBERCULOSIS. Eighty-nine cases of mammary tuberculosis are reported in the literature since 1904. To these we add 5 personally observed cases. Six of the 27 cases collected by Scott from the records of St. Bartholomew's Hospital lacked microscopic confirmation of the diagnosis. These together with 3 cases reported by St. Jacques, 4 cases reported by Braendle, 3 by Hardouin and Marquis, 2 by Fraenkle, and 2 reported by Carr are not included. Of the remaining 74 cases, 45 are classified as primary and 29 as secondary in type. Scott's series, notwithstanding the elimination, remains the largest as yet reported, while our experience (5 cases) has not been exceeded by that of any individual operator. These 5 cases occurred among a series of 600 operative cases of mammary disease (1898 to 1913), and we do not recall having seen another instance of the disease in thirty-five years of surgical practice. This low ratio (less than 1 per cent. for all

cases, or 2.5 per cent. for the benign breast lesions) is in decided contrast to the observation of Bloodgood, who found tubercular mastitis in 6 per cent. of the cases of benign lesions of the breast admitted to the Johns Hopkins Hospital. The average relative frequency is more nearly approached in the list of cases collected by Sidney Scott, as follows:

Acute mastitis (abscess)	380	} 1890 to 1903, 1.31 per cent.
Chronic mastitis	79	
Benign tumors and cysts	296	
Malignant disease	1051	
Tuberculosis	24	
<hr/>		1830

Anspach accepts the 30 cases considered by Bartsch as primary among the latter series of 65 collected cases, and adds 12 cases from the literature of the succeeding three years, 1901 to 1904. Therefore, were it not for the uncertainty of determination of the primarity of mammary tuberculosis, we would be surprised at the statement of von Eberts, who, in 1909, accepted only 40 of the cases reported since Dubar's contribution in 1881 as true examples of a primary manifestation of the disease. We have accepted the 42 cases collected by Anspach and added 45 cases, making a total of 87 cases of primary tuberculosis of the breast reported since 1881. With the exception of cases of concurrent carcinoma and tuberculosis which we have considered separately, our review of the literature is complete. The meagre number of cases (45) reported over a period of nine years (1904 to 1913), when compared with the general morbidity of tuberculosis and a yearly mortality of 5,000,000 of people from this disease, proves the extreme rarity of tubercular infection of the breast.

PREDISPOSING CAUSES. *Sex.* Tubercular mastitis almost invariably occurs in the female. Only 10 male cases are recorded. Heyfelder reported the first case occurring in the male in 1851. Since then Delbert, Ferguson, Ressiguie, Poirier, Hebb, Schede, Demme, Parsons, and Khesin have each observed a case.

We have included Ressiguie's case among the list of primary infection, while Parsons' case is clearly secondary to tubercular osteitis. The third case reported since 1904, that of Khesin, was secondary to tubercular infection of the knee-joint. Scudder rejects those cases in the male reported by Horteloupe and Heyfelder.

Age. The youngest patient in our series, a girl of fourteen, was operated upon by Abraham; the oldest a widow, aged sixty-four years, by Ingier. Both Scudder and von Eberts remark that the patient of Remy and Noel, a woman, aged fifty-four years, is the oldest case on record. The cases of Geissler, Ingier, and Scott in our series exceed this age. No case of tubercular mastitis in the

female has been observed before the age of puberty, and the oldest case on record is that reported by Shields, in a woman aged seventy-three years. Demme reports a case the result of direct inoculation in a male infant, four days old.

The following tables prove the correctness of von Eberts' statement that "the period of reproductive activity embraces the vast majority of cases."

AGE INCIDENCE.

PRIMARY CASES.		SECONDARY CASES.	
10 to 20 years . . .	1	10 to 20 years . . .	4
20 to 30 years . . .	10	20 to 30 years . . .	9
30 to 40 years . . .	15	30 to 40 years . . .	8
40 to 50 years . . .	12	40 to 50 years . . .	4
50 to 60 years . . .	4	50 to 60 years . . .	3
60 to 70 years . . .	2	60 to 70 years . . .	1
Not mentioned . . .	1		
	<hr/> 45		<hr/> 29

60.9 per cent.

41.9 per cent.

These tables also disprove the assertion of the older writers and of more recent observers, among others St. Jacques, that tuberculosis of the breast is a disease of adolescence and young womanhood.

SOCIAL CONDITION.

PRIMARY CASES.		SECONDARY CASES.	
Single	6	Parous	23 or 51.1 per cent.
Married	29	Nulliparous	21
Widows	2	Males	1
Males	1		<hr/> 45
Not mentioned . . .	7		
	<hr/> 45		

PRIMARY CASES.		SECONDARY CASES.	
Single	7	Parous	8 or 27.5 per cent.
Married	16 or 53.5 per cent.	Nulliparous	19
Widows	0	Males	2
Males	2		<hr/> 29
Not mentioned . . .	4		
	<hr/> 29		

Whether the influence of fecundity as indicated by the above tables acts in the role of a real predisposing cause, or that it is merely coincident to the age at which the disease is more likely to occur, is difficult to answer. The statistics of Anspach's 40 primary cases are as follows:

Married	28 or 70.0 per cent.
Single	12 or 30.0 per cent.
Parous	19 or 47.5 per cent.

These figures, it will be observed, closely correspond with those in the list of primary cases in our series. It is unjustifiable to draw conclusions from so small a number of cases, yet it would seem that the mammary changes incident to pregnancy are not more predisposing to tubercular involvement of the breast from a distant focus than to the so-called primary involvement. At least were such predisposition potent in the production of tubercular mastitis we would expect to find many more cases among the thousands of nulliparous women suffering with various forms of tuberculosis, active or latent. Von Eberts says that "lactation is possibly the most important predisposing cause of tubercular mastitis." That many factors concur in reducing the tissue vitality to the point of tubercular predisposition is true of the breast as of other tissues, and no one factor stands out prominently in this capacity.

Heredity. A tubercular family history was elicited from 4 of our secondary cases and from 3 of the primary cases. The influence of heredity in the production of tuberculosis of the breast, as elsewhere, acts merely in the role of a contributing cause.

Trauma. Traumatic injury to the breast is rarely followed by tubercular infection. Schley quotes Poirier, Hebb, Sabrazes, and Binaud, who observed cases preceded by injury. In 5 of the primary cases of the present series trauma seemed influential in the tubercular process. These cases have been observed by Wannenwenhuysse, Marangonii, Abraham, Scott and ourselves. In Marangonii's case a violent injury was received five years before the development of the tuberculosis, which was also preceded by suppurative mastitis. The latter occurred two years after receipt of the injury, which was looked upon as causal.

Scott's case is of particular interest: The patient, a woman, aged thirty-four years, accidentally pierced her left breast with a needle. Suppuration followed. The needle was removed, but a sinus persisted, with increasing induration around it, and involvement of the axillary glands. Tuberculosis was found on microscopic section of the involved area.

Demme noticed the development of tuberculosis in a preformed sinus, the latter a sequel of simple pyogenic mastitis.

Slight trauma is more likely to be followed by tuberculosis in susceptible persons than is violent injury. This view is of general application in surgical tuberculosis, especially of the bones and joints; but there is no reason for believing it true of mammary tuberculosis. Abraham, however, looked upon his case as a result of slight injury. A latent focus of tuberculosis in the breast, as in other tissues may be incited to activity by traumatism. If the trauma is violent the overlying tissues suffer immediate ulceration in the absence of abscess formation, as illustrated in one of our secondary cases (Case No. 27). The usual result, however, is the production of an active tuberculosis which eventuates in abscess formation, the residual abscess of Sir Stephen Paget.

Antecedent Mastitis. Six (13.3 per cent.) of the primary cases gave a history of suppurative mastitis. This antedated the tubercular process, one, two, two, five, eleven, and thirty-seven years respectively. Of those cases collected by von Eberts in which the gland had functionated, there was a history of inflammation complicating lactation in 42 per cent, with suppuration in 20 per cent. Scudder accepts 53 of the reported cases as primary tubercular mastitis, and states that half of the patients had borne children and that 10 (18.8 per cent.) had previous attacks of mastitis. He remarks that mastitis (pyogenic) is more common in the tuberculous than in the normal puerperium. Schmidt's case, included in our list of secondary cases, illustrates the coincident appearance of tubercular and acute pyogenic mastitis in the puerperium. The patient, aged twenty-three years, noticed a small nodule on the left forearm in the summer of 1904. She was confined in November, 1904, and a few days later developed acute mastitis on the right side. An abscess opened spontaneously, leaving fistulas, which failed to heal. She was admitted to Schmidt's clinic in March, 1905.

Examination showed a fluctuating swelling the size of an orange on the left forearm. The right breast was enlarged, hard, and nodular, and showed five fistulous openings in the areola. Both axillæ contained enlarged lymph nodes. Both the tumor of the forearm and the mastitis were proved to be tubercular at operation. The possibility of local tubercular infection of a preformed sinus is to be remembered.

SYMPTOMATOLOGY (INITIAL SYMPTOMS).

PRIMARY CASES.

Lump	29 or 68.8 per cent.
Tender lump	3
Hardening	1
Abscess breaking spontaneously	1
Discharge from the nipple	1
Pain	4 or 8.8 per cent.
Swelling after traumatic injury	1
Pain and hardening	2
Not mentioned	3
	<hr/>
	45

SECONDARY CASES.

Lump	21 or 75.0 per cent.
Lump in neck and breast	1
Acute puerperal mastitis	1
Pain	2 or 6.9 per cent.
Lump in breast and pain on respiration	1
Hardening of the nipple and slight pain	1
Not mentioned	1
Lump in axilla	1

The most frequent initial symptom of tubercular mastitis is a painless lump. In 78 per cent. of the malignant and 86 per cent. of the benign mammary neoplasms operated on by us this was likewise the first sign of the disease. Pain, it will be observed is an infrequent initiative sign, although it occurs more often during the course of the disease. 17 of our primary and 9 of the secondary cases suffered with pain. But this was slight, rarely referred, and was especially noted during the stage of abscess formation and just prior to rupture. These figures refute the statement of Scudder that "pain is an early and constant symptom, often severe in type, and affecting 50 per cent. of cases." Any patient presenting a lump in the breast and complaining of pain on respiration in the region of the tumor should be skiagraphed for osteitis of the underlying ribs. The difficulties of diagnosis of tubercular mastitis resulting from contiguous bone disease should be in this wise eliminated. Beyond this, the value of pain as a differential diagnostic index is practically *nil*. Retraction of the nipple was rated by Dubrueil, Verneuil, and Warden as the first indication of tuberculosis of the breast occurring in their respective cases eleven months, two years, and five years before a mass was palpable.

COURSE OF THE DISEASE. The average duration of the disease in the primary cases was 10.1 months, in the secondary cases, 11.2 months. Tuberculosis of the breast runs a much more rapid course than carcinoma of the breast. In our series of the latter condition, thirty months elapsed on the average from the time of onset to the date of operation. In one of Marangonii's cases the disease was of four years' duration. Geissler and ourselves have observed cases in which the patients came to operation less than a month from the time of appearance of the initial symptoms. The rapidity of the disease process, changes in the size and consistence of the tumor mass, early fistula formation, early involvement of the axillary lymphatics, and, in a few instances, pain, bring the great majority of the subjects of tubercular mastitis to the surgeon within the first year of the disease. Tenderness, usually slight, is noticed in the later stages, but like the other subjective symptoms offers little aid in differential diagnosis.

GENERAL CONDITION OF THE PATIENT. It is surprising to find that the larger number of our primary cases occurred in robust women. In the secondary cases also, in spite of additional foci of tuberculosis, little mention is made of marked systemic effect. Tubercular mastitis is not only compatible with but usually associated with excellent general health.

PHYSICAL SIGNS (LOCATION):

PRIMARY CASES.

Under nipple	4
Upper outer quadrant (only 4 associated with palpable axillary enlargement)	10
Lower inner quadrant	1
Above the nipple	1
Lower outer quadrant	6
To the outer side of the nipple	1
Upper outer and upper inner quadrant	2
Below the nipple	1
Generalized	1
Not mentioned	13
Upper outer and above the nipple	2
Near the nipple	2
Above and below the nipple	1
Peripheral	1
	<hr/>
	45

SECONDARY CASES.

To the outer side of the nipple	2
Upper outer quadrant	8
Generalized	3
Above the nipple	6
Below the nipple	3
Under the nipple	2
Lower outer quadrant	1
Lower inner quadrant	1
Not mentioned	3
	<hr/>
	29

SIDE INVOLVED.

PRIMARY CASES.

Left	15
Right	22
Bilateral	1
Not mentioned	7
	<hr/>
	45

SECONDARY CASES.

Left	13
Right	15
Not mentioned	1
	<hr/>
	29

CONDITION OF THE SKIN.

PRIMARY CASES.

Involvement of the skin:

Adherent	3
Red and tender	1
Red and adherent	1
Adherent at areola	1
Darkened	1
Dimpled	1
Adherent and discolored at site of fistula	10
	<hr/>
	18
Normal	27
	<hr/>
	45

SECONDARY CASES.

Involvement of skin:	
Ulcerated area in the axilla	2
Adherent	6
Reddened	3
Adherent and ulcerated	6
Hard and discolored	1
Abscesses of the skin	1
	—
	19
Normal	10
	—
	29

FISTULAS.

PRIMARY CASES.

Present in 14 cases or 31.1 per cent.
Multiple in 3 cases.

SECONDARY CASES.

Present in 13 cases or 44.7 per cent.

CONDITION OF THE NIPPLE.

PRIMARY CASES.

Retraction (1 bilateral)	19 or 42.2 per cent.
Ulcerated	3
Discharge from nipple:	
Brown colored	1
Serous	2
Not mentioned	1
	—
Normal	24

SECONDARY CASES.

Retraction	9 or 32.1 per cent.
Discharge from the nipple (purulent)	1
Normal	20

PALPABLE ENLARGEMENT OF THE AXILLARY LYMPH NODES.

PRIMARY CASES.

25 cases 55.5 per cent.

In 1 case a palpable cord connected
the breast tumor with the axillary
nodes.

SECONDARY CASES.

21 cases 72.4 per cent.
6 bilateral.

In 2 cases a palpable cord connected
the breast tumor with the axillary
nodes.

The presence of fistulas, retraction of the nipple, and enlarged axillary glands is a triad strongly suggestive of tubercular mastitis. Scudder found fistulas present in over 50 per cent. of cases, and states that nearly all cases had axillary tuberculosis. The following statistics from Scott's series of 27 cases are given for their comparative value:

Fistulas present in 10 cases, or 35 per cent.

Definite history of injury in 1 case.

Acute onset in 2 cases.

Skin adherent in 2 cases, or 70 per cent.

Nipple retracted in 10 cases, or 30 per cent.

Axillary glands enlarged in 17 cases, or 60 per cent.

LYMPH-NODE INVOLVEMENT. The lymph nodes of the side corresponding to the lesion were enlarged in 60.9 per cent. of our primary cases and in 75 per cent. of our secondary cases. Von Eberts estimates the frequency in primary cases at 75 per cent. The enlargement may be a simple hyperplastic adenitis, but the microscopic examinations in the present series were too few to estimate the proportion with accuracy.

Tubercular axillary lymph adenitis of the opposite side may possibly occur by way of the lymph channel described by Poirier, arising in the lower inner quadrant of the breast and going to the opposite axilla in the plane of the deep fascia without traversing the opposite breast. Secondary infection of the tubercular areas of the breast with pyogenic bacteria occasionally takes place as a result of blood infection from other pyogenic foci in the body, but usually results from extraneous infection after the spontaneous rupture of a tubercular abscess, or the unclean surgical opening of such collection.

We know of no case in which violent septicemia followed secondary infection, as not infrequently occurs in tubercular abscesses of other organs.

PATHOLOGICAL TYPES OF MAMMARY TUBERCULOSIS. Tuberculosis of the breast may be classified as follows: (1) Acute milary tubercular mastitis. (2) Nodular (discrete, disseminated, confluent), tubercular mastitis. (3) Sclerosing tubercular mastitis (Scott) (comparable to fibroid phthisis). (4) Mastitis tuberculosa obliterans (Ingier). (5) Various atypical forms.

NODULAR VARIETY. The great majority of cases of mammary tuberculosis are of the discreet, nodular variety. The tubercular process is fundamentally the same in all organs, but in the breasts presents variations as the result of the histological peculiarities of these structures. The bacilli lodge in the stroma in the majority of cases and incite a localized tubercle formation. Daughter tubercles form at the periphery of the original focus, and in time, usually a matter of several months, sometimes longer, a palpable mass is formed. This varies in size, but rarely exceeds that of a hen's egg. As a rule, it remains unattached to the structures underlying the breast, and the overlying skin is not involved until late in the disease. The mass is of irregular contour, poorly defined, and slightly tender. It is of irregular consistence, and certain areas almost without exception show softening, often with fluctuation. If the inflammatory reaction is marked, sclerotic tissue contraction causes retraction of the nipple, especially if the mass is centrally located. The clinical course varies, depending upon the secondary changes in the nodule. In most cases the skin becomes adherent, often at the periphery of the areola; it assumes a dark red color, with final pointing and spontaneous rupture of the abscess or abscesses a permanent sinus remains, as a rule, around

which the tubercular tissue can be felt as a nodular column. Progression of the disease results in further abscess and sinus formation. Frequently the disease remains quiescent or the sinuses may heal. It is in the former stage that the patient is often first seen by the surgeon. On the other hand, nature may wall off the primary nodule and cause its cicatrization, with permanent cure, or the process may remain latent for years, with ultimate remanifestation. Finally the caseation and liquefaction of the focus may be quite complete, but so well walled off that rupture is impossible. In some instances this sclerotic wall may reach a thickness of one and a half inches or more. The result is an abscess in which we see no reason for differentiation from the intraglandular cold abscess of Roux; it is simply a terminal stage of the discreet nodular variety.

DISSEMINATED NODULAR VARIETY. As illustrative of this type of the disease, we can offer no better description than that given of Marangonii's case.

The patient, a woman, aged twenty-nine years, began having pain in her left breast soon after weaning her second child. The breast became enlarged and hard, and at the same time the axillary glands also enlarged. On examination the left breast was found enlarged, diffusely nodular, and exquisitely tender. Marangonii's notes of the pathological features were as follows:

"The entire gland is covered with nodules. The lesion is very diffuse, so that only very few lobules are of normal structure for the most part; the less altered areas are situated near the periphery of the organ. An advanced sclerosis of the connective tissue is present. The sudoriparous glands beneath the connective tissue are enlarged and cystic. Epithelial proliferation of both the ductal and acinous epithelium is marked." In this the much rarer form of nodular tuberculosis of the breast the disease is more rapid in development and rarely becomes quiescent.

As with Marangonii's case, this type of the disease is seen most frequently during lactation. In the confluent variety of mammary tuberculosis the nodules run a rapid course to caseation and liquefaction. The abscess is often centrally located and lacks the tendency of the discreet, nodular variety to peripheral spreading. Schley considers this the usual mode of formation of the "interglandular cold abscess" of Roux.

SCLEROSING TUBERCULAR MASTITIS (SCOTT). In 10 of Scott's 27 cases the prominent pathological feature was a diffuse sclerosis. In 3 of these cases an overlying sclerosis hid deep abscesses, while in four others, superficial abscesses were found overlying areas of marked sclerosis. From the remaining 3 cases solid tumors were removed. These latter cases were considered carcinomatous until microscopic examination revealed tuberculosis. It is to cases of the latter type that we would limit the term sclerosing tubercular mastitis. Sclerosis is a feature of almost every case of nodular

tuberculosis, but like fibroid phthisis, there is a pathological entity among tubercle infections of the breast in which instead of tubercle formation there occurs a diffuse epithelioid and embryonic connective-tissue infiltration from which Langhan's giant cells are wanting and in which the process is essentially sclerotic. As Scott remarks, this type is seen most often in patients advanced in years. The breast in the terminal stage of this condition is small, hard, and deformed. Differential diagnosis from scirrhus is impossible. Demonstration of the tubercle bacillus in stained tissue sections is the only absolute means of diagnosis.

MASTITIS TUBERCULOSA OBLITERANS. Ingier has recently described a case in which the inflammation was confined to the walls of the excretory ducts and periacinous connective tissue, with slight involvement of the interlobular stroma. Granulation tissue involved the membrana propria of the finer ducts and acini from without. In the larger ducts the process seemed to arise within the duct walls. Detachment of the epithelium resulted, with final obliteration of the lumina of the ducts. Tubercle bacilli were found in fluid expressed from the cut surface of the tumor.

The nipple had ulcerated away and the case seemed illustrative of primary ductal infection.

VARIOUS ATYPICAL FORMS. Cases such as the one in our list in which the disease began in a nodule resembling a sebaceous cyst are to be considered atypical. Poirier describes a case in which two small cutaneous vesicles developed into indurated tubercular nodules. In Orthmon's case a subcutaneous infection resembling a furuncle first appeared, with subsequent induration and extension of its base. These with other cases already referred to are to be considered atypical, and are very rare manifestations of the disease.

CONCURRENCE OF TUBERCULOSIS AND CARCINOMA OF THE BREAST. Klose has collected 17 cases of this rare combination of pathological processes, although some of these cases were not proved microscopically. The author gives the notes of a personally observed case in detail, and quotes Franco, who has seen 2 cases. The author further quotes Kellenberger, who saw secondary cancer in the tubercular breast of a woman. Scheidigger operated on a woman whose father, two sisters, and a brother died of tuberculosis, and whose mother died of cancer of the uterus. The tumor, which was the size of a plum, consisted of adenocarcinomatous tissue, with inclusion of typical tuberculosis. The axillary glands contained areas of tuberculosis but no carcinoma. The most recent reports are by Rodman and Bauer. Berger reports a most unique case. The patient, a woman, aged forty-seven years, noticed a hard, movable tumor in the upper outer quadrant of the left breast. A hardened cord connected the tumor with the enlarged and tender ganglia in the axilla. The tumor of the breast was scirrhus in character, while the axillary glands were found to be tubercular.

BACTERIOLOGIC DIAGNOSIS. Zironi and von Eberts have grown the tubercle bacillus in culture from breast lesions. Ingier and Schley found the bacillus in stained smears. Fuller, Brandsburg, and Stromberg demonstrated the organism in stained tissue sections. The foregoing are included in our list of primary cases. Among the secondary cases is that of Duvergey, the diagnosis was confirmed by finding the tubercle bacillus in smears of pus. Delfino and Mantelli reports the only instances of positive animal inoculation from tubercular breasts since 1904. In Mantelli's case (No. 35, primary series) the diagnosis was made by guinea-pig inoculation with pus aspirated from a breast abscess. Davis found tubercle bacilli in the discharge from the nipple of a case of tubercular mastitis.

DIFFERENTIAL DIAGNOSIS. When tubercular mastitis has progressed to the stage of fistula formation, the usual termination of all except the sclerotic varieties, it must be differentiated from simple pyogenic mastitis of a subacute or chronic form, broken-down gummas, and actinomycosis. The two latter conditions are exceedingly rare, although Shattock calls attention to the necessity of distinguishing between syphilis and tuberculosis. We have not met with a case in our studies in which either condition was suspected before or found at operation undertaken on the diagnosis of tuberculosis. When the history or the presence of another lesion raises the question of the gummatous nature of a breast lesion, the Wassermann reaction will prove or disprove the presence of the disease. In the event of a positive blood test, the effect of antileptic treatment will demonstrate the nature of the breast lesion. The discharge from a broken-down actinomycosis contains the ray fungus. Only 5 or 6 cases are recorded.

The differentiation of subacute or chronic pyogenic mastitis, either of the true chronic abscess type, or one in which fistulas have formed, from the similar varieties of primary tuberculosis is impossible, except by laboratory methods. Sclerosing tuberculosis of the breast, especially in the absence of areas of degeneration gives, in certain cases, all of the classical symptoms of carcinoma, from which it cannot be differentiated clinically.

The preoperative diagnosis in this class of cases in our list was invariably cancer. These mistakes are unfortunate, since less radical measures than total excision effect a cure in mammary tuberculosis. Tumors of the breast giving the typical physical signs of fibro-epithelial tumors, simple cysts, and sarcomas will not excite suspicion of a tubercular origin. Revel reports a case of cystic adenofibroma associated with tuberculosis. In these rare cases the presence of inflammatory signs arising in a preëxistent tumor and in the axillary nodes offers aid in the diagnosis. The tuberculin test should be of value in keeping with its diagnostic value in tuberculosis of other organs. Von Eberts insists upon its use for diagnostic purposes, but we can find no reference to its

employment in mammary tuberculosis. Frozen section diagnosis of all doubtful tumors should be made at the time of operation. This may prevent unnecessary mutilation in mammary tuberculosis in young women, for we are assured that in the ordinary case less radical procedures than those employed in the past will serve to cure tuberculosis of the breast.

Reference has already been made to bacteriological methods of diagnosis. The use of the x-ray will, as mentioned above, serve to diagnose a primary focus in an adjacent rib.

PROGNOSIS. No reported case of mammary tuberculosis died as the result of operation. All of the cases in our series were operated upon with one exception, and all were discharged from the hospital apparently cured except a case operated upon by Mantelli, in which a sinus persisted. Stromberg and Robinson report recurrences. Braendle reports 4 cases alive and well thirteen years, eleven years, nine years, and eight years, post operationem, respectively. In one of Schley's cases there was no return of the disease after four years, and Fuller observed cases three and eight years with no sign of recurrence. Von Eberts' case was well six months after operation. Of Anspach's 12 cases, 4 were well one year after operation, 3 not heard from, and 1 died at the end of three years (cause unknown), while the others remained well eight, four, three, and two years respectively. Few cases of recurrence have been reported. These cases presented pulmonary lesions as a rule. In several instances tubercular peritonitis, meningitis, or acute miliary tuberculosis manifested itself usually some years after operation. Operative treatment as carried out in the past offers, in the primary cases, almost complete assurance of permanent cure. The prognosis in the secondary form of mammary tuberculosis depends entirely upon the activity, location, and extent of the primary focus.

TREATMENT. The treatment in all of our primary cases was operative. The methods of operation were as follows:

PRIMARY CASES.

Simple amputation of the breast and curettage of the axilla	10
Simple amputation of the breast	13
Wet dressings for fifteen days, with incision of the abscess	1
Exploratory incision (diagnosed cancer), with radical operation	4
Incision followed by excision of the mass	4
Incision followed by excision of the mass and axillary nodes	2
Excision of the tumor and a portion of the pectoralis major muscle	1
Simple amputation of the breast, with removal of a portion of the pectoralis major muscle	2
Excision of the mass in the left breast, incision and curettage of abscess in the right breast	1
Simple amputation of the breast, followed by tuberculin, 1 to 1500 mg. every ten, days	1
Excision of the tumor	2
Radical amputation	3
Simple amputation of the breast and removal of pectoral fascia and the axillary lymph nodes	1

SECONDARY CASES.

Incision followed by excision of the involved quadrant	1
Excision of the involved quadrant and axillary nodes	5
Incision followed by radical excision of the breast	1
Simple amputation of the breast with excision of the axillary glands	11
Radical excision of the breast (1 by Tausini's method)	3
Simple amputation of the breast	3
Incision and curettage of the abscess	1
Not operated	1
Excision of mass in breast and curettage of involved ribs	2
Amputation of the breast and pectoralis major muscle. Scraping of rib. Serum treatment	1
	<hr/> 29

These tables represent the opinions of those who have had experience in the treatment of mammary tuberculosis. The uniformly good results would seem to justify continuance in their use. Von Eberts advises tuberculin therapy in early cases, in the absence of mixed infection, and when the probability of lactation can be safely ruled out. We know of no case in which this form of treatment has been used, and in the future would advise excision of a localized tubercular mass in the breast of a young woman, with exploration of the axilla in the presence of palpable lymph nodes. In older women simple amputation with excision of the axillary nodes is the method of choice. In either case tuberculin should be given, since this in proper dosage can do no harm and may perhaps aid nature in overcoming any small focus that might easily escape the knife. Conservatism had better be expressed in limiting the area of excision than in discarding operative treatment.

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CASES OF MAMMARY TUBERCULOSIS (PRIMARY TYPE) REPORTED IN THE

Case.	Reported by.	Year.	Sex.	Age.	Social condition.	Children.	Side involved.	Fistulas, sinuses.	Duration.	Size.	Location of tumor (quadrant).	Pain.	Condition of skin.	Nipple.		Palpable enlargement of axillary glands.
														Retraction.	Discharge from.	
1	Scott	1904	F	41	M	1	R	...	2 mos.	Chestnut	Lower outer	...	Adherent	+
2	Scott	1904	F	45	M	13	R	+	6 wks.	...	Beneath nipple	...	Adherent and discolored	+	...	+
3	Scott	1904	F	47	Widow	3	L	...	3 mos.	1 in. in diameter	Lower outer
4	Scott	1904	F	38	M	4	L	...	3 mos.	Walnut; getting smaller	Outer	...	For 1 wk. red and slightly tender	+	+	+
5	Scott	1904	F	42	M	1	R	..	18 mos.	1½ in. in diameter	Beneath nipple	..	Adherent	+	+
6	Scott	1904	F	36	M	8	R	..	10 wks.	2 in. in diameter	Upper outer and upper inner	..	Red and adherent	+	+
7	Scott	1904	F	41	M	5	R	+	9 mos.	Marble	...	Began 6 wks ago	Adherent veins enlarged	+	...	+
8	Scott	1904	F	34	L	+	+
9	Scott	1904	F	60	M	2	1 yr.	Hen's egg	Upper outer and above nipple	+
10	Scott	1904	F	34	M	6	R	..	2 mos.	...	Lower outer	Recently	..	+	...	+
11	Scott	1904	F	38	M	...	R	...	1 mo.	Small lump	Near nipple	+
12	Braendle	1906	F	36	M	9	L	+	5 mos.	Hazel nut	Under nipple	Occasionally shooting	Discolored and adherent	+
13	Braendle	1906	F	23	M	2	R	+	3 yrs. healed and 4 mos. broken down again	Nut	Upper outer	...	Adherent at sinuses	+
14	Braendle	1906	F	38	M	2	L	+	3 mos.	Entire breast enlarged	Lower inner	Lately	Adherent at sinuses	+	...	+
15	Braendle	1906	F	34	M	...	R	+	5 wks.; 3 wks. ago opened; 10 days ago again opened 4 mos.	Entire breast enlarged	Fistulas above and below nipple	...	Adherent and discolored at sinuses	+
16	Geissler	1906	F	50	R
17	Geissler	1906	F	56	R	...	2 wks.	Hen's egg	Upper outer	+
18	Berger	1906	F	47	Upper outer	+
19	Zironi	1907	F	23	M	2 mis-carriages	L	...	1 yr.	...	Upper outer	Tenderness	...	+

LITERATURE SINCE 1904, INCLUDING TWO PERSONALLY OBSERVED CASES.

Initial symptoms.	Heredity.	Antecedent condition of breast.	General health.	General physical examination.	Treatment.	Result.	Pathology: microscopic.	Tubercle bacilli found.	Animal inoculation.
Lump	Mother and 1 child died of tuberculosis	Negative	Exploratory incision; diagnosed cancer. Radical operation	...	Tuberculosis		
Lump	...	Suppurative mastitis twice	Fine	Strong obese woman	Diagnosed as suppurative mastitis and scirrus; radical operation	...	Tuberculosis; lymph nodes		
Lump	Husband and father died of tuberculosis	...	Fine	Negative	Incision; pus evacuated; swelling excised	...	Tuberculosis		
Lump	...	Cough for several weeks	Fine	Negative	Incision; pus evacuated; excision of involved area	...	Tuberculosis		
Discharge from nipple	Negative	Incision, pus evacuated; excision of involved area	Wound healed by first intention	Tuberculosis		
Lump	Negative	Incision; 1 oz. of pus evacuated; 10 days later excision of involved area and axillary glands	...	Tuberculosis		
Lump	Brother died of tuberculosis	Had poultices applied and two abscesses burst	...	Negative	Excision of a portion for frozen section; simple amputation	...	Tuberculosis		
Lump	..	Needle in breast followed by infection and persistent sinus	Good	Negative	Simple amputation	Uneventful recovery	Tuberculosis		
Lump	...	Acute mastitis at age of 23 yrs.	Good	Negative	Excision of lump and axillary glands	Uneventful recovery	Tuberculosis; lymph nodes		
Lump	...	Abscess of right breast after birth of 3d child; retracted nipple since	Good	Negative	Incision of abscess; radical amputation.	Uneventful recovery	Tuberculosis		
Lump	Good	Negative	Radical incision	Uneventful recovery	Tuberculosis		
Lump	...	Left breast never functionated	Robust	Negative	Simple amputation; excision of axillary nodes	Alive and well 13 yrs. later	Tuberculosis		
Abscess opened spontaneously	...	Nursed children at left breast	Good	Negative	Simple amputation	Alive and well 11 yrs. later	Tuberculosis		
Lump	Good	Negative	Simple amputation	Alive and well 9 yrs. later	Tuberculosis		
Hardening of breast	...	Mastitis 2 yrs. before	Good	Negative	Simple amputation	Alive and well 8 yrs. later	Tuberculosis		
Lump	Good	Negative	Amputation	Uneventful recovery	Tuberculosis		
Lump	Good	Negative	Amputation	Uneventful recovery	Tuberculosis		
...	Good	Negative	Amputation	Uneventful recovery	Tuberculosis; sclerotic lymph nodes		
Tenderness and enlargement	Good	Negative	Amputation of breast and curettage of axilla	Alive and well 2 yrs. later	Tuberculosis	In culture	

CASES OF MAMMARY TUBERCULOSIS

Case.	Reported by.	Year.	Sex.	Age.	Social Condition.	Children.	Side involved.	Fistulas, sinuses.	Duration.	Size.	Location of tumor (quadrant).	Pain.	Condition of skin.	Nipple.		Palpable enlargement of axillary glands.
														Retraction.	Discharge from.	
20	Marangonii	1907	F	41	M	+ In lower part of areola	5 yrs.	.	Lower	..	Adherent and discolored	+	...	+
21	Marangonii	1907	F	29	M	6	R	.	.	Large lump	Generalized	+	+
22	Hardouin	1907	F	32	M	1	R	...	2 mos.	...	Above nipple	Shooting pain	Tenderness	+
23	Revel	1908	F	45	S	0	L	..	Few mos.	Nut	Periphery	+
24	Brandsburg	1908	F	30	M	0	L	...	6 yrs.	Hen's egg	+	+ Ulcerated suppurative	+
25	Brandsburg	1908	F	34	M	4	R	...	2 mos.	Hen's egg	...	+ Especially in nipple	...	+	+ Ulcerated	+
26	Ressiguie	1909	M	40	..	.	R	.	3 mos.	Horse-chestnut	Near nipple	At times
27	Fuller	1909	F	35	M	5	..	+ Under nipple	1 yr.	Egg	Upper outer	.	Adherent and discolored	+	..	+
28	Fuller	1909	F	50	M	2	Bi-lateral	+ In left breast	1 yr.	...	Upper outer, L.; upper inner, R.	.	Adherent and discolored
29	Von Eberts	1909	F	24	S	...	R	..	1 yr.	Pigeon's egg	Lower outer	+	...	+
30	Khesin	1909	F	54	S	...	L	...	3 mos.	+
31	Stromberg	1909	F	32	M	3	R	...	3 yrs.	+	Adherent	+
32	Ingier	1910	F	64	Widow	+	...	Hen's egg	Ulcerated away	...
33	Schley	1910	F	R	Mandarin orange	Upper outer	...	Adherent and discolored
34	Mantelli	1910	F	33	M	...	L	+	...	Hazelnut	...	+
35	Mantelli	1910	F	25	S	...	R	...	3 mos.	Egg	Upper outer	+
36	Mantelli	1910	F	45	M	4	R	...	6 mos.	+

(PRIMARY TYPE).—Continued.

Initial symptoms.	Heredity.	Antecedent condition of breast.	General health.	General physical examination.	Treatment.	Result.	Pathology; microscopic.	Tubercle bacilli found.	Animal inoculation.
Swelling after trauma; abscess opened 3 yrs. later	...	Violent trauma 5 yrs. ago, followed by suppurative mastitis 3 yrs. ago	Poor	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis; lymph nodes		
Piercing pain in breast	Good	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis		
Pain and lump	Good	Negative	Wet dressing for 15 days; incision of abscess	Recovery uneventful	Tuberculosis of a portion of abscess wall		
Lump	Robust	Negative	Simple amputation; curettage of axilla	Recovery uneventful	Tuberculosis; lymph nodes		
Lump	Good	Negative	Simple amputation	...	Tuberculosis	In stained tissue sections	
Lump	...	11 yrs. ago suppurative mastitis; 2 mos. ago present condition began	Poor	Negative	Radical excision	...	Tuberculosis	In stained tissue sections	
Lump	Good	Negative	Simple amputation with removal of portion of involved P. major muscle	...	Tuberculosis		
Lump	...	Abscess lanced 2 yrs. ago	Good	Negative	Excision of involved area	Well 3 yrs. after operation	Tuberculosis; frozen section		
Lump	Good	Negative	Excision of mass in left breast; incision and curettage of abscess in right breast	Well 8 yrs. after operation	Tuberculosis; frozen section	In stained tissue sections	
Lump	...	5 yrs. ago abscess of breast opened spontaneously and discharged for 4 mos., since when has been closed	Good	Negative	Simple amputation; tuberculin, $\frac{1}{1500}$ mg. every 10 days	Well 6 mos. after operation	Tuberculosis; lymph nodes	Grown in pure culture from breast lesion	
Lump	Good	Negative	Simple amputation and cleansing of axilla	Fistula persisted for some months	Tuberculosis		
Pain and induration	...	Operated 3 yrs. ago for similar condition; disease immediately recurred	Poor	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis	In stained tissue sections	
Ingiev describes the pathology of this case and calls it tuberculosa obliterans. He refers to 2 similar cases, 1 a fibrosis mastitis of tubercular origin in a lactating breast.				Negative	Simple amputation	...	Tuberculosis	Found in smears of pus	
Lump	Fine	Negative	Simple amputation	Well 4 yrs. after operation	Tuberculosis	Found in smears of pus	
Pain and lump	Good	Negative	Iodine locally followed by excision of nodule	...	Tuberculosis	...	Guinea-pig inoculation positive
Lump	Good	Negative	Aspiration; guinea-pig inoculation with pus positive; simple amputation of breast and cleansing of axilla	...	Tuberculosis	...	Diagnosed by injecting pus from abscess into guinea-pig
Lump	Good	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis	Found in tissue section	

CASES OF MAMMARY TUBERCULOSIS

Case.	Reported by.	Year.	Sex.	Age.	Social condition.	Children.	Side involved.	Fistulas, sinuses.	Duration.	Size.	Location of tumor (quadrant).	Pain.	Condition of skin.	Nipple.		Palpable enlargement of axillary glands.
														Retraction.	Discharge from.	
37	Mantelli	1910	F	25	S	...	L	...	1½ yrs.	Mandarin orange
38	Abraham	1910	F	25	M	2	L	...	1 yr.	Fist	Upper outer	...	Adherent to areolar area	+
39	Wannienwenhuysee	1911	F	32	14 mos.	Pea	Under nipple	Recently	+
40	Carr	1911	F	17	M	1	6 mos.	Orange	Outer	+	+
41	Robinson	1911	F	21	S	...	L	...	7 mos.	+	+	...
42	Cope	1912	F	22	M	2	L	...	2½ yrs.	Orange
43	Powers	1913	F	23	L	+	Lower outer	+
44	Deaver	1913	F	47	M	..	R	...	3 wks.	Small lump	Upper outer	+	...	+	+	...
45	Deaver	1913	F	44	M	...	R	+	3 yrs.	Egg	Upper outer	+	Adherent and ulcerated	+	scroous	...

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(PRIMARY TYPE)—*Continued.*

Initial symptoms.	Heredit.	Antecedent condition of breast.	General health.	General physical examination.	Treatment.	Result.	Pathology, microscopic.	Tubercle bacilli found.	Animal inoculation.
...	...	Operated 1½ yrs. ago for lump in left breast; fistula remained 3 mos.; immediately recurred	Good	Negative	Excision of lump	Fistula remained	Tuberculosis		
Lump	...	Slight trauma	Good	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis		
Lump	...	Trauma	...	Negative	Excision of the tumor and a portion of the P. major muscle which was involved	...	Tuberculosis		
Tender lump	Good	Negative	Simple amputation and cleansing of axilla	...	Tuberculosis		
Pain	...	Operated on April, 1911; tumor 5 cm. in diameter removed from left breast	Good	Negative	Radical excision	...	Tuberculosis		
Lump	Good	Negative	Excision of tumor	...	Tuberculosis		
Lump	Negative	Amputation of breast; removal of deep pectoral fascia and axillary lymph nodes	...	Tuberculosis		
Pain	...	Trauma 1 yr. ago	Fine	Negative	Simple amputation	...	Tuberculosis		
Pain	Good	Negative	Simple amputation	...	Tuberculosis		

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CASES OF MAMMARY TUBERCULOSIS (SECONDARY TYPE) REPORTED IN THE LITERATURE

Case.	Reported by.	Year.	Sex.	Age.	Social condition.	Children.	Side involved.	Fistulas, sinuses.	Duration.	Size.	Location of tumor (quadrant).	Pain.	Condition of skin.	Nipple.		Palpable enlargement of axillary glands.
														Retraction.	Discharge from.	
1	Scott	1904	F	44	M	...	L	...	6 wks.	1½ in. in diameter	Outer	+	...	+ Bilateral
2	Scott	1904	F	26	M	1	R	..	3 wks.	Ill-defined	Upper outer	...	Ulcerated area in right axilla	+ Bilateral. In right axilla an ulcer overlies the enlarged gland
3	Scott	1904	F	37	M	...	L	..	1 yr.	...	Entire breast	...	Adherent	+	...	+ Indurated cord running from breast to to axilla
4	Scott	1904	F	38	M	...	R	...	3 wks.	Pigeon's egg	Upper	+	Red and inflamed	+	...	+ Bilateral
5	Scott	1904	F	38	S	..	R	Ulcer in axilla	6 wks.	...	Upper outer	+	Adherent and ulcerated in axilla	+
6	Thurston	1904	F	36	R	+	4 mos.	..	Upper outer	...	Adherent	+ Bilateral
7	Schmidt	1905	F	23	M	2	R	+	5 mos.	...	Generalized	+	Multiple sinuses	+	...	+ Bilateral
8	Braendle	1906	F	36	M	1 alive and well. Several died of tuberculosis in infancy	R	+	1 yr.	...	Upper half	...	Adherent	+
9	Braendle	1906	F	54	M	9	R	+	1 yr.	...	Above nipple	...	Adherent	+ Bilateral
10	Braendle	1906	F	43	M	8	R	...	9 wks.	Walnut	Upper outer	Enlarged in sub-clavicular region
11	Delfino	1906	F	22	M	...	L	+	10 mos.; 4 mos. ago ulcerated	...	Lower outer and upper outer	...	Involved at fistulous openings	+ Appeared after breast tumor
12	Geissler	1906	F	60	M	9	L	...	4 wks.	L breast 3 times size of right	Generalized	..	Hard and discolored	+
13	Bahuand	1906	F	18	S	...	L	+	6 mos.	2; 1 in areola	Lower	...	Adherent at areas of fistulas	+
14	Parsons	1907	M	38	L	...	3 mos.	4x5x1½ inches	Under nipple	...	Abscesses of skin; adherent to both superficial and deep structures	+
15	Marangoni	1907	F	20	L	...	1 yr.	Small egg	Lower outer	...	Adherent	+	...	+ Indurated, running from breast to axilla

SINCE 1904 (ANSPACH'S PAPER), INCLUDING THREE PERSONALLY OBSERVED CASES.

Initial symptoms.	Heredity.	Antecedent condition of breast.	General health.	General physical examination.	Treatment.	Result.	Pathology; microscopic.	Tubercle bacilli found.	Animal inoculation.
Lump	...	Left breast functionless owing to congenitally retracted nipple. Occurred during lactation	Good	Negative	Incision; evacuation of pus and curds of milk. Excision of involved quadrant	...	Tuberculosis		
Lump	...	Consolidation (tubercular) apex of right lung	...	Enlarged cervical glands; pulmonary tuberculosis	Excision of upper outer quadrant of right breast and axillary nodes	...	Tuberculosis		
Lump	Enlarged glands above clavicle	Exploratory incision; evacuation of pus. Radical excision	...	Tuberculosis; lymph nodes		
Lump	...	Occurred during lactation; nipple congenitally ill-formed	Good	Negative	Simple amputation with excision of axillary glands	Uneventful recovery	Tuberculosis		
Lump	Father died of tuberculosis	Had tuberculosis of jaw and bones of forearm in childhood	Good	Scars of healed lesions	Radical excision	Uneventful recovery	Tuberculosis		
Lump	Excision of area around sinus and axillary gland	...	Tuberculosis; lymph nodes		
Acute puerperal mastitis	Mother died of tuberculosis	Acute puerperal mastitis; one year ago noticed nodule on forearm	...	Fluctuating abscess of forearm	Simple amputation	...	Tuberculosis		
Lump	Good	Lump size of goose egg in left cervical region	Amputation of breast and cleansing of axilla	Alive and well 1 yr. after operation	Tuberculosis		
Lump in neck and breast	Fair	...	Amputation of breast and cleansing of axilla	Alive and well 1 yr. after operation	Tuberculosis		
Lump	...	Operated on 6 yrs. ago for suppurative glands in right axilla	Fair	...	Amputation of breast and cleansing of axilla	Alive and well 1 yr. after operation	Tuberculosis; lymph nodes		
Lump	...	Pulmonary tuberculosis	...	Pulmonary tuberculosis	Amputation of breast and curettage of axilla	Uneventful recovery	Tuberculosis	...	Guinea-pig inoculation positive
Induration and lump	...	Pulmonary tuberculosis	...	Pulmonary tuberculosis	Simple amputation	...	Tuberculosis		
Pain	Father, mother, 1 brother and several sisters died of tuberculosis	Tuberculosis of jaw (lower) and cervical nodes	...	Pulmonary tuberculosis	Simple amputation and curettage of axilla	...	Tuberculosis		
Lump and pain on respiration	Amputation of breast and P. major muscle; scraping of ribs; serum treatment	...	Tuberculosis in scrapings from ribs		
Lump in left axilla	...	Axillary tuberculosis	Amputation of breast and cleansing of axilla	...	Tuberculosis		

CASES OF MAMMARY TUBERCULOSIS

Case.	Reported by.	Year.	Sex.	Age.	Social condition.	Children.	Side involved.	Fistulas, sinuses.	Duration.	Size.	Location of tumor (quadrant).	Pain.	Condition of skin.	Nipple.		Palpable enlargement of axillary glands.
														Retraction.	Discharge from.	
16	Maranganii	1907	F	22	M	2	L	...	4 yrs.; 6 mos. ago breast tumor developed	Egg	Below nipple and lower inner	Slight	...	+	Pus	+
17	Hardauin and Marquis	1908	F	20	S	...	R	...	1 yr.	Orange
18	Brandsburg	1908	F	24	M	...	L	...	3 mos.	Hen's egg	Upper outer	+
19	Linty	1909	F	40	L	...	2 mos.	...	Under nipple	+
20	Khesin	1909	M	23	R	+	+
21	Cignozzi	1910	F	17	S	This is a case of mammary tuberculosis, the result of a primary axillary adenitis of tubercular origin. The author quotes it as an indication for the Tansini method of radical excision of the breast.				
22	Abraham	1910	F	14	S	...	L	+	2 yrs.	8 cm. in diameter	Upper	Slight recently	Red and adherent	+
23	Montelli	1910	F	52	M	..	R	+	5 mos.	Orange	Upper	...	Adherent
24	Duvergey	1911	F	48	M	..	L	+	6 mas.	...	Above nipple	...	+	+
								Following incision								
25	Vignard and Pasquier	1912	F	35	M	3	L	+	8 mos.	Goose egg	Upper outer	...	Reddening	+
26	Powers	1913	F	15	S	...	R	+	6 mos.	...	Upper outer	Entire axilla filled with lumpy mass
27	Deaver	1913	F	54	M	...	R	+	1 yr.	...	Upper outer	+	Adherent and ulcerated
28	Deaver	1913	F	26	S	..	R	...	4 mas.	Egg	Lower	+
29	Deaver	1913	F	31	R	...	2 yrs.	Fist	Lower inner	+	Adherent and ulcerated	+

(SECONDARY TYPE)—*Continued.*

Initial symptoms.	Heredit.	Antecedent condition of breast	General health.	General physical examination.	Treatment.	Result.	Pathology; microscopic.	Tubercle bacilli found.	Animal inoculation.
Harden- ing of nipple and slight pain	...	Axillary adenitis; operated on 4 yrs. ago	Simple amputation and cleansing of axilla	...	Tuber- culosis		
Lump	...	Pleurisy 4 yrs. ago	Simple amputation	Unevent- ful re- covery	Tuber- culosis		
Lump	...	Abscess for past 3 yrs. in left axilla; opened spon- taneously, leaving sinuses	Fair	Axillary adenitis	Amputation of breast and cleansing of axilla	Well 3½ yrs. after operation	Tuber- culosis	T. B. in stained tissue sections	
Lump	...	Pulmonary tuberculosis	...	Pulmon- ary tuber- culosis	Halstead amputation	...	Tuber- culosis		
Lump	...	Leg amputated for tuber- culosis of knee; ascribes trouble in breast to trauma	...	Antece- dent joint tuber- culosis	Simple amputation and cleansing of axilla	...	Tuber- culosis		
...	...	Enlarged cervical glands since age of 10; 2 yrs. ago operated on for enlarged glands in left axilla	Tausini's method of radical excision	...	Tuber- culosis		
Lump	...	Pain in the hip for 2 yrs.	...	Negative	Incision along lower mar- gin of the breast; curet- tage of tumor mass	...	Tuber- culosis		
Lump	...	Antecedent pleurisy; purulent mastitis years ago	...	Negative	Simple amputation	...	Tuber- culosis		
Pain	...	Sept., 1910, infected (left hand) finger while wash- ing clothes in tubercu- losis hospital; opened, drained and healed. In April 1911 had lost weight and developed axillary abscess which opened in May and left a sinus	...	Pulmon- ary tuber- culosis; 2 ulcers of breast. Ulcer in subcla- vicular fossa; multiple fistulas	Not operated	T. B. found in pus	
Lump	...	In June, '11, had tubercular abscess of palmar surface of left thumb, opened and also had epitrochlear and axillary node involvement	Partial excision of breast and curettage of axilla	...	Tuber- culosis		
Lump	Negative	Upper outer quadrant of breast excised; axilla cleaned; glands adherent to axillary vein; tuber- culin post operation	Well several months later	Areas of tuber- culosis found in overlying skin		
Lump	...	Trauma caused lump to ulcerate	Good	Enlarged glands in left supra- clavicular triangle	Excision of involved area of breast; excision of en- larged glands	Dis- charged in good condition	Tuber- culosis		
Lump	...	Abscesses of ear, back, etc.; pain on deep breath- ing in breast	Good	...	Excision of cyst in breast; scraping of ribs	Dis- charged in good condition	Tuber- culosis		
Lump	Father died of tubercu- losis	Good	...	Simple excision revealing sinus leading to rib; scrap- ing of rib	Dis- charged in good condition	Tuber- culosis		

DENTAL SEPSIS: ITS RELATION TO THE SYSTEM.¹

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THE cases upon which the following observations are based presented purulent infection in and about the teeth. The terms used in literature to indicate this condition are oral sepsis, Riggs' disease, pyorrhea alveolaris, dental sepsis, dental abscess, necrosis, etc. By the internist these terms are very loosely used, and one must turn to works upon dentistry to get any accurate information of the nature and extent of the *local* process. Even in such works, however, there is no adequate explanation of the relation of these variously situated foci to each other. Works on internal medicine contain as yet no comprehensive discussion of this subject, and its causative relation to some of the most destructive systemic processes (arthritis, endocarditis, etc.), a relationship which we know to be of primary importance in the consideration of the etiology, diagnosis, and therapeutics of these conditions. It is the duty of the internist to familiarize himself with this focus of pyogenic infection *in its early stage* and to coöperate with the dentist as with the surgeon in the eradication of foci of pus in any part of the body. The teeth, especially at the pulp, may, like the tonsillar, peritonsillar, and deep urethral tissues, harbor pyogenic organisms and even small amounts of virulent pus without local manifestations, although systemic manifestations having apparently no relation to this source appear from time to time, and may reach a crippling or fatal degree. It is this latent or subtle quality in the local infection which causes it to be frequently overlooked or discounted by the internist. Such foci can often be detected by radiographic examination only. In one instance (Case I) the only manifestation was a slight crepitation of the left temporo-maxillary joint, which was unaccompanied by pain or tenderness. There was slight ear pain, for which the patient consulted an aurist. This, and the unusual sound in opening and closing the jaw, was the only complaint. The radiograph showed a pulp abscess. The tooth was removed and a pure culture of *Streptococcus viridans* was obtained from the pulp, socket, and gum, and the blood gave positive complement fixation for the same organism. There was no fever at any time and no leukocytosis. Vaccines were prepared from this tooth, but were not used at the time, as conditions did not seem to justify doing so. A few months later general arthritis developed and the autogenous vaccine was imme-

¹ Presented at the meeting of the Association of American Physicians held at Washington, D. C., May, 1913. (See Transactions of the Association of American Physicians, 1913.)

diately employed, with marked benefit, but not with entire disappearance of the arthritic manifestations. The blood still showed positive fixation for the same organism. On further search, another tooth was found, with small pus focus, and on removal of this there was rapid improvement, with ultimate disappearance of the arthritis. The manifestations of arthritis were pain on motion, active and passive, and slight tenderness on deep palpation, but no redness or local fever. The knees, ankles, wrists, elbows, and small joints of the hand were involved. The temporomaxillary joint was, however, the only one permanently damaged, and in consequence the crepitation persists (see case reports, Case I). This case well illustrates the slow, steady absorption, with destruction, unless the focus is detected and the process checked. It is always possible in the protracted cases in which no removal of the focus or other checking of the infection is carried out, for new foci to develop in the joints or soft tissues. Under these circumstances the condition may become progressive, consequent to but independent of the original focus and often hopelessly destructive to the joints or visceral tissues. The persistence of the temporomaxillary joint signs in the case just cited makes it possible that here may be a new focus of infection which may appear in other localities later. Several such new foci, even though the original focus has been drastically treated by removal of the tooth and by curettement, make the clinical problem one of difficulty, disheartening the patient and baffling the physician. Vaccines under these circumstances are the only rational therapeutic remedy. This case demonstrates the importance of close coöperation between dentist and internist. This obligation to coöperate rests as much with the dentist, if not more so, as with the internist. The dentist may find a tooth abscess with which, in most instances, he deals mechanically. Later the internist sees the same case, and though he may associate the history of the diseased tooth with the sytemic disturbance which he now finds, it is often impossible, at that late date, to accurately correlate the two processes. The dentist in most instances does not make cultural studies of the pus, and thus the only opportunity of detecting the invading organism and of preparing vaccines may be lost. If, as seems likely, vaccines prove to be the only certain means of combating these destructive pyogenic infections in their advanced stages, the loss of the opportunity to procure this important therapeutic agent would be a serious and culpable omission.

Setting aside the question as to whether the dental involvement is the cause or effect of a general sepsis, the clinical fact remains that the material procurable from such foci frequently offers the only, and often brief, opportunity to identify the invading organism and of procuring materials from which vaccines may be made. I prefer to emphasize this feature of the subject, which is of so great

diagnostic and therapeutic importance, rather than that of cause and effect, which, as a question of etiology, involves problems possibly unsolvable. The cases upon which this report is based have been studied in coöperation with Drs. M. I. Schamberg, Alexander Currie, W. D. Tracy, Harold S. Vaughan, dentists of New York City, three of whom are also graduates in medicine. Among the radiographs accompanying this article I have included those of cases which have come under the personal observation of these dentists through whose courtesy I am enabled to reproduce them here.

In using the term coöperation I do not mean to infer that the patients were told to consult the dentist merely, but I accompanied them to the dentist's office and studied with him the radiographs and local conditions. I believe such consultation to be as necessary as those common between surgeon and internist. When a pyogenic dental infection requiring liberation of the pus existed, arrangements were made for bacteriological specimens to be procured at the dentist's office, and later, if conditions indicated, a specimen of blood for culture and complement fixation tests was taken. A certain number of dentists are in accord with this practice: indeed, a small number have gone beyond the medical practitioner, and without his coöperation are studying cases with just such thoroughness as outlined above. There is, however, among the dentists a large class of dental tinkerers, who practice upon the easy persuasibility of the public. A large mass of mechanical work is thus done upon the teeth with often an entire neglect of the destructive focus of pus. A specific instance of this occurred in Case II. In this case there were (see case reports, Case II) areas of pus from which *Streptococcus viridans* in pure culture were obtained. These areas of pus were detected only by the radiograph, there being but slight local symptoms or signs. Into the roof of the mouth of this patient a dentist had inserted an elliptically curved bar of metal as large as the lead of a pencil, with possibly some idea of correcting a dental displacement, but with no correction of the pus focus. Subsequently this patient developed a cervical spondylitis, which cleared up shortly after draining the abscess cavities. One may even go farther and state that some of this mechanical work entraps pus which before such interference was draining into the mouth cavity, and thus at least lessening systemic absorption. Crown-work and filling are two common pieces of mechanical work which, if improperly done, may be a means of thus entrapping pus. A cavity in which a small quantity of pus is allowed to remain may harbor virulent organisms, which slowly extend the inflammation to the surrounding tissues, setting up large abscesses with active systemic absorption. Case IV illustrates the action of imperfect filling by producing irritation and inflammation (see case reports, Case IV). The radiograph in this case showed a

shadow which was thought to be a pus area, but proved to be only thickening of the tissues. Cultures from all the suspected areas and from the root of the imperfectly filled tooth (which was drawn) were negative. There was, however, a positive fixation in the blood for three out of twelve strains of *Streptococcus viridans*. Four months prior there had been an acute abscess of a tooth not connected with this imperfect filling, but severe enough to cause pain and swelling and to require radical treatment. No cultures were taken at the time of the operation, but the positive fixation found later and the inflamed areas about to become purulent were significant. This case seems to fall into a group of cases of latent streptococcic infection in which faulty dental work would be a sufficient exciting cause to establish an active local process, with systemic absorption. The faulty dental technique in crown, filling, and other mechanical work here referred to is well known to dentists, and it is mentioned not as an arraignment of the dental profession, but for the information of the general practitioner. It may be further stated that so far from being at fault, the dentists must be given the credit of pioneer work in dealing radically with pyogenic infection in and about the teeth and in the use of radiography in detecting such conditions. Evidence of this is found in the writings of such dentists as A. Witzel,² L. C. Ingersoll,³ W. J. Reese,⁴ Louis Jack, C. N. Pierce,⁵ and many others who published their observations between the years 1880 and 1900. While these were general considerations following the initial communication of John W. Riggs, of Hartford, Conn., which was made in October, 1875, they all showed an appreciation between these local dental conditions and systemic disturbances. The later writings of such dentists as M. I. Schamberg,⁶ formerly of Philadelphia; Harold S. Vaughan,⁷ of New York; Thomas L. Gilmer,⁸ of Chicago, to mention a few only, show an even greater appreciation of a probable relation between oral sepsis and many serious systemic diseases, an appreciation not yet shown by the majority of general practitioners. Among medical men, William Hunter,⁹ of London, and the late Dr. Kinnicutt,¹⁰ of New York, have been in recent years the most active in bringing before the medical profession the importance of this subject.

There are two chief factors militating against the thorough investigation and prompt treatment of these cases:

¹ Vierteljahresschrift f. Zahnheilkunde, 1882; British Jour. Den. Sci., xxv, 153.

² Ohio State Jour. Dent. Sci., 1881, i, 189.

³ Dental Cosmos, 1886, xxv, 550.

⁴ International Journal, 1892, 1894 and 1895, xiii, xv and xvi.

⁵ Dental Cosmos, January, 1906; Dental Brief, June, 1906.

⁶ Jour. Allied Dent. Sci., March, 1913. (In this communication Vaughan shows the infection to be due to Vincent's bacteria without typical pus pockets.)

⁷ Illinois Med. Jour., March, 1912.

⁸ British Med. Jour., July, 1900.

⁹ Proc. Roy. Soc. Med., April, 1913, vol. vi, Sup. No. 7, May, 1913.

1. The dentist and the internist, through the improved standards of dental work, are coming together more and more in consultation and coöperation. This was, however, not always the case, and recalls the relation which existed between the surgeon and physician in England in the days of coffee-house consultation, in which the druggist was the middleman. The physician in those days merited his lower position in the scientific world, and the surgeon justly felt that these doctor druggists were not men worthy to coöperate with. As the internist built up his diagnosis upon scientific research, it became possible for the surgeon to meet with him and study the case. Such is true also of the dental profession, and in 1904 the science had reached such a degree of accuracy that a section of dental surgery was established in the British Medical Association,¹¹ in which dentist and physician participate. Throughout the country today there is developing a class of dentists whose opinions are based upon carefully weighed evidence, and who are devising and carrying out operative measures as delicate in technique as some of the more important surgical operations. This first factor against the proper care of these cases can be best removed by the direct consultation between dentist and internist and their continued coöperation in the care of the case.

2. The second factor is the tenacity with which men and women alike will insist upon retaining rotten fangs in the mouth. The dentist regards the loss of a tooth as the internist does the death of a patient, and in this opinion the dentist has the insistent support of the patient. It is not an exaggeration to say that in saving certain teeth, the dentist may be condemning the patient to a living death through subsequent crippling arthritic infection or actual death through septic invasion of some vital organ. This factor can best be removed by educating the public, through the medium of the internist and dentist, to the realization of the seriousness of these conditions. When this is correctly understood by the patient, the removal of the offending teeth will be as readily consented to as tonsillotomy or the opening of a mastoid. Dr. Hunter,¹² has dealt very thoroughly with the obligation of the dentist in this matter, and his opinions are warmly supported by many of the best dentists. I believe, however, that some of his remarks may be taken with great directness by the internist, who is not infrequently the first under whose observation these cases come.

REPORT OF CASES.

CASE I.—W. W., female, aged thirty-five years. Married. April, 1912, complained of pain in the left ear, for which she was

¹¹ British Med. Jour., November 19, 1904.

¹² Practitioner, December, 1900.

referred to a specialist, who reported subacute inflammation of the left Eustachian tube. She was under treatment for this from time to time during the summer, but her condition not improving, she consulted, of her own accord, another specialist and was told by him that he found nothing wrong with the throat, ear, or nose, and by him was referred back to me. October 7, 1912, the patient seen again by me, when the following notes were made.

Complaint. Pain and tenderness located in the left ear. Distinctly audible crepitation of the left temporomaxillary joint.

Family History. Negative, except that one brother, aged forty-five years, is a victim of arthritis deformans, which began about nine years ago. He was acutely ill for several months, and while the joint condition was not progressive, he had occasional attacks of fever. He had been seen by several of the prominent consultants of this country. One sister (also under my care) has had septic infection of an antrum, for which she was treated by a specialist. Another sister had involvement of the small joints of the hands about the same time that the brother became infected.

Past History. Presented nothing of importance, except that wine was taken freely with meals and at other times also. The patient had one child. There was no history of miscarriages or pelvic infection.

Physical Examination. Presented nothing of importance that has not already been given. The patient was slender and of nervous temperament.

BLOOD EXAMINATION.

Hemoglobin (Fleischl)	78 per cent.
Red cells	5,200,000
White cells	7,400

DIFFERENTIAL COUNT OF WHITE CELLS.

Polynuclear neutrophiles	78 per cent.
Transitional cells	0 "
Large mononuclear cells	1 "
Large lymphocytes	0 "
Small lymphocytes	19 "
Eosinophiles	2 "
Mast cells	0 "
	—
	100 "

Urine examination was negative.

October 12, 1912, the patient was seen in consultation with Dr. Currie (dentist), and radiographs of the temporomaxillary joint and teeth were studied. Nothing was observed in the joint, but suspicion was directed to a tooth, which it was determined to remove. In the socket and about the pulp of this tooth pus was found, cultures from which were taken by Dr. Hastings at the time of its removal. Bacteriological report was as follows: Cul-

tures from the tooth, the tissue, and from the tooth socket gave pure *Streptococcus viridans*, and cultures from pus about the gum and about the tooth gave *Streptococcus viridans* and *Staphylococcus aureus*. A blood culture taken a few days later showed no bacteremia, but for seven strains of streptococci the fixation was negative for four strains, and positive for three strains of *Streptococcus viridans*. There was no fixation for the gonococcus, and the blood for lues was negative. We had, therefore, evidences of a local *Streptococcus viridans* abscess, with systemic absorption. That the temporomaxillary involvement was a manifestation of this sepsis was a reasonable conclusion, borne out by subsequent developments. The cultures were preserved for the purpose of employing vaccines at a later date should the removal of this tooth and a cleansing of the socket not prove curative, or should other joints show evidences of infection. The patient continued under general observation, with marked improvement of the ear condition. The crepitation of the temporomaxillary joint continued, but without pain or tenderness. In November, 1912, the patient went West, where she remained about two weeks. During this time she experienced, for the first time, pain in the ankles, knees, and wrists. There was no swelling, redness, or other local signs. On her return to New York, in the latter part of November, 1912, the pain continued in the joints noted, and extended to some of the finger-joints and to three toes of the right foot. The pain was worse in damp weather. This condition became sufficiently severe to alarm her, and on December 27 she reported to me. There was no fever and no local signs, except slight tenderness on moving the larger joints and on pressing some of the smaller joints. There was pain for the first time in the left temporomaxillary joint. There had been no chills or sweating. The knee-jerks were present. The pupils reacted normally, and there was no Romberg. It was decided to begin vaccine, and she received her first inoculation January 9, 1913. Up to April 21 she received twenty inoculations. By March 31, except for slight pain in a toe-joint of the right foot, the joints were free of all symptoms, a condition which up to that date had existed for about three weeks. She felt better than she had at any time for several years. The details of the vaccine therapy are omitted. By April 14, 1913, the patient complained of considerable tingling in the legs, and swelling and puffing of the feet. There was no fever, and though she had maintained her weight, and her appetite was good, she looked badly. April 21 she complained of feeling wretchedly; joints were more sensitive, and she noticed puffiness of the feet, especially at night. The diet and hygienic surroundings were carefully regulated and a tonic was prescribed and the vaccines were increased. She however continued to do badly. Blood examination showed the following:

BLOOD EXAMINATION.

Hemoglobin	100 per cent. (Sahli corrected)
Red-blood cells	4,720,000
White-blood cells	9,000

COLOR INDEX 1. DIFFERENTIAL COUNT.

Polynuclears	71 per cent. (300 counted)
Lymphocytes	19.6 "
Large mononuclears	5 "
Transitionals	3.6 "
Eosinophiles	0.6 "
Red-blood cells normal	

Blood negative for organisms, but the complement fixation was positive for the same strains of *Streptococcus viridans* as in the test made October, 1912.

On May 7 the teeth were again thoroughly radiographed, and though a careful study of these by two dentists and myself failed to detect pus shadows, Dr. Currie discovered a small area of pus near a devitalized tooth adjoining the seat of original infection. There was also impingement of a neighboring tooth, which accounted possibly for the pain. This tooth was removed and the area thoroughly curetted, when rapid improvement followed. The local pain entirely disappeared, and in two or three weeks the joints gradually ceased to cause trouble. The general health improved and except for occasional observations by the dentist the case passed from medical attention. The crepitation in the left temporomaxillary joint persisted, and had been sufficiently marked to be audible to those sitting nearby. This joint, therefore, was probably permanently damaged.

CASE II.—W. R., male, aged forty-four years, married; seen May 27, 1913; complained of pain and tenderness in the vertebral column about opposite the seventh cervical.

Past History. Presented nothing of importance. Had no children, and wife had had no miscarriages. Used alcohol and tobacco in moderation. Gave an indefinite history of some trouble with the knee-joint, which he attributed to trauma two years before; occasionally felt slight twinges of pain in this knee on motion. Had had slight pain at times in some of the toe-joints. Was an active business man.

Present History. Vertebral trouble began about January, 1913; not progressive and not noticeable when sitting or lying still. Up to June, 1912, took recreation in boxing, but since then on account of the neck condition, had not been able to do so. At times he feared to move because of the pain. In every other particular his general health was good.

Examination. A large, well-built, healthy looking man; dark complexioned, of American-German parentage. There was no

pigmentation of the mucous membrane, and the skin pigmentation was uniformly distributed. Carried his head in a fixed position, suggesting "stiff neck." On lightly tapping the top of the head tenderness was localized to about the sixth cervical vertebra, at which point the pain was localized; there was also here well-marked tenderness on pressure. A radiograph disclosed no definite change at this articulation.

BLOOD EXAMINATION.

Hemoglobin (Fleischl)	85 per cent.
Red cells	6,016,000
White cells	6,000

DIFFERENTIAL COUNT.

Polynuclear	62 per cent.
Large lymphocytes	4 "
Small lymphocytes	26 "
Eosinophiles	3 "
Transitional cells	5 "
	—
	100 "

Radiographs of the teeth were studied with the dentist, Dr. Currie, and suspicion was directed to the upper right canine and the upper incisor (see Figs. 2 and 6); in addition the dentist detected discharging pus from the upper right canine. On dealing with these teeth radically, pyorrhea, with marked destruction of the alveolus of the upper right canine, which was discharging, was found; also central necrosis of the right upper incisor, which, in Dr. Currie's opinion, was of some duration, together with a pus pocket in the lower left molar under an imperfectly fitting crown. Cultures by Dr. Mann gave *Streptococcus viridans*. The offending teeth were removed and all the infected areas thoroughly cleaned out. Tonic treatment was at the same time instituted. One week after this radical treatment the condition of the neck, which had existed for five months, markedly improved, and by the end of June entirely disappeared. This case had been under the observation of a dentist, who was consulted for the routine care of the teeth, and who entirely overlooked the purulent condition, inserting in the mouth the badly fitting crown and a bar for the correction of a suspected displacement.

CASE III.—J. J., female, aged forty years; married. Seen September, 1911. Pain and tenderness in left knee-joint.

Past History. Nothing of importance. Borne two healthy children; no miscarriages. Had been in uncertain health for some years, but condition was attributed to nervousness, nothing definite manifesting itself.

Present History. The present trouble began with pain and tenderness on the outer aspect of the left knee-joint, aggravated by

walking. This joint was treated locally by an orthopedist, and after eight months of wearing a brace and being under general tonic treatment, baths, etc., other joints became painful, including the temporomaxillary joints, making the chewing of food and articulation difficult. One year after the initial knee condition, fever of an irregular type appeared. Eighteen months from the onset an intermittent odor of the breath was noticed, and this first attracted attention to the teeth, which had given only such signs as were considered common and unimportant. On thorough examination of the mouth, pus was found to exude from the gum about a molar tooth, which, being removed, disclosed a pus cavity in the gum, from which was obtained a dram of pus. From this pure culture of *Streptococcus viridans* was obtained. The jawbone was found to be partly involved in the purulent process. The patient sustained a typhoid temperature for four months, with the involvement of many of the large and small joints. Autogenous vaccine was used continuously over a period of three years. During this time phlebitis in one leg developed. For ten months there has been steady improvement in the general condition, but several of the joints seem permanently damaged, and the knee-joints are fixed (by a possible tendon or muscle shortening) at an angle of 45 degrees. This case will be published elsewhere in detail from the bacteriological, vaccine, and arthritis viewpoints. For this reason the above brief outline only is given.

CASE IV.—C. S., widow, aged forty-two years; complained of malaise, indigestion, and broken sleep.

Family History. Unimportant.

Past History. Showed repeated attacks of pharyngitis, and an acute attack of nephritis, without known cause, four years ago. Had not been robust for eight or ten years, but never confined to bed. Twenty-five years before a prominent specialist diagnosed a tuberculous apex in the right lung. From this she seemed to have entirely recovered. Appendicitis with operation six years before. Two years before had amenorrhea for several months. Menses had been normal for over a year. Four months before, while travelling, developed a painful swelling over an upper left molar. This was treated by a dentist seen in the emergency, and he drained away a considerable amount of pus and directed her to see her dentist as soon as possible.

Present history dates from November 27, 1912, with complaint of pus about a molar four months before, as given above, but there is no trouble with the teeth at present. Patient was always an active woman, attending to her own affairs, but is now unable to go about without prostrating fatigue. Appetite is poor, and she sleeps but a few hours at night. For the first time in her life she finds relief in remaining in bed.

Examination. Skin pale, but mucous membrane of fairly good color. Chest negative except for soft systolic blow over the heart. Abdomen negative. Over both lower extremities were pinhead, purpuric spots. There had at no time been any joint pain or tenderness.

BLOOD EXAMINATION. DECEMBER 2, 1912.

Hemoglobin	90 per cent.
Red-blood corpuscles	5,600,000

DIFFERENTIAL COUNT.

Polymorphonuclears	61 per cent.
Transitionals	5 "
Lymphocytes	24 "
Large mononuclears	7 "
Eosinophiles	3 "

Urine Examination. Reaction, acid; sugar, none; pus, none; albumin, faintest possible trace; urea, 1 per cent.; casts, none; specific gravity, 1.018.

Blood Culture. Negative for organisms (agar and broth) for twelve strains of streptococci; the fixation was positive for three.

Examination of the Teeth. Pyorrhea pocket (see Figs. 2, 3 and 4) about a twelve-year molar. At the root of a filled tooth the radiograph showed a shadow, thought to be due to pus. Tooth was removed and filling was found to be incomplete, and from this inflammation extended into the surrounding tissues. Cultures from this area were negative. The shadow in the radiograph was due to thickening of the bone and peridental membrane, secondary to the inflammation. Though the cultures from the tooth were negative, the blood showed positive fixation for three out of twelve strains of *Streptococcus viridans*, and had this local condition remained untreated, an abscess would undoubtedly have developed, as was the case with the other side of the mouth four months previous.

This and Case II perhaps represent an early stage of a local streptococcic infection with systemic manifestations. In both cases the systemic manifestations rapidly disappeared after thorough local treatment. Such cases require careful watching for the possible development of new areas of infection.

CASE V.¹³—R. S., female, aged thirty years, unmarried; seen February, 1913, complaining of severe pain localized to the left tonsillar region and left ear. The pain radiates toward the mastoid and the neck posterior to the sternocleido muscle, with a centre

¹³ This case represents a class well-known to dentists, but one with which general practitioners are usually unfamiliar. It is introduced here, however, for the information of the general practitioner in order that he may distinguish it from beginning dental sepsis, with which it can be readily confused.

apparently in the external auditory canal. A thorough examination of the throat and ear by a specialist revealed nothing. There was no fever. The teeth were found to be exceptionally good. There was, however, tenderness on slight pressure on the gum below and posterior to the lower left third molar; the gum was slightly red and puffy. Conditions suggested an abscess, but the radiograph revealed a wisdom tooth impinging directly upon the molar and crowding that tooth (see Fig. 1). This condition, known in dentistry as "impaction," is a frequent cause of reflex pain, and without the use of the radiograph leads to much surmise with regard to possible mastoid and middle-ear disease, retrotonsillar, deep gum, and dental abscesses. These cases are frequently treated by lancing the gum in the hope of liberating supposedly entrapped pus. The loss of sleep on account of the pain and disturbed digestion not infrequently lead to the impression of a systemic condition secondary to the supposed abscess. This case was surgically treated by Dr. Schamberg, who removed the offending tooth after which the patient was entirely relieved.

SUMMARY. These cases are selected as representing five important features of general disturbance of the system, secondary to dental disease. In the first case, the dental disease was detected in part and the organism determined before the joint complications developed. The use of autogenous vaccine in this case would seem to have held the progress of the disease in check, but not until all of the pus areas in the teeth had been cleaned out did the systemic condition show a permanent improvement. The system, however, was probably under the influence of toxic absorption for some months before radical measures were instituted. In such cases there is always a possibility of new and independent foci of infection having been set up. Such a stage in the development of the disease precludes the possibility of checking it by dealing with the original focus merely, and it would seem here that vaccines are our only means of combating the infection. This is true of Case III, in which neither the organism was detected nor the autogenous vaccine employed until many months after the system had been under the influence of the infection and many joints involved, but this case also represents the ravages of septic infection of dental origin unchecked, as was common with all cases before the teeth were suspected as the original focus. Cases II and III represent possibly the earliest stage in the systemic manifestation of absorption of toxins from a dental source. Case V represents a class in which mechanical disturbance may be mistaken for an inflammatory process. From these cases and others the following symptoms and signs may be classified. In attempting a classification, it should be stated that cases of this type have not, as yet, been studied by internists and dentists together sufficiently to make such a classification complete. It should also be stated that there are a number

of characteristics which may prove of great clinical value when corroborated by thorough observation, but which for lack of such corroboration are omitted here. Such, for example, are the association of joint involvements in which the upper jaw is the seat of pyogenic infection in contradistinction to an adenitis and burrowing pus when the lower jaw is involved. Again, what degree of alveolar destruction is necessary before systemic absorption takes place? Also, is there any relation between tonsillar and peritonsillar and faucial infections and dental disease? In this connection, Dr. Vaughan's¹⁴ observations with regard to Vincent's bacteria and dental disease are pertinent. We are as yet without any conclusive studies on the lymphatic system draining such areas.

SYMPTOMS. Malaise, indigestion, fetor of the breath, often intermittent; there may be periods in which the breath is so offensive as to be noticeable some little distance from the patient, while at other times such fetor cannot be detected by careful search. This is frequently called attention to by others, and is rarely noticed by the patient. Loosening of the teeth, which may also be intermittent. Tenderness of the teeth on chewing; an indefinable aching of the gums; pain referred to the ear (internal and external), the mastoid, the cheek bone, the eyes, and fauces. Rapid and sometimes copious loss of hair, which may occur intermittently. All the frank manifestations, such as acute pain and swelling, which immediately attract attention to the teeth, are omitted here, though of course they come into this classification.

SIGNS. A brick-red tinge about a sixteenth of an inch in width at the dentogingival margin, quite distinct from the whitish-red color of the healthy gum, marks areas of infection. These areas bleed readily on slight pressure. If a wooden spatula is run along the gum margin the diseased portions can frequently be detected by the bleeding-points left in the wake of such pressure. In more advanced cases a diseased tooth, from loosening, can be moved in its socket; a healthy tooth is absolutely immobile. Again, the gross signs, such as destruction of the cemental portions, surface necroses, and visible discharge of pus, together with more obscure signs requiring instrumental examination by a dentist, are not mentioned here in detail, though they of course belong under this head. The most important point in connection with both symptoms and signs is that manifestations of systemic involvement may appear without there being any symptom referable to the teeth in which actively absorbing pus areas may be present. Such systemic manifestations, however, show marked improvement, and sometimes completely disappear with the radical removal of the septic focus. Paramount among these systemic manifestations are arthritis and phlebitis. It is a noteworthy fact, however, that not until an overwhelming

¹⁴ H. S. Vaughan, Jour. Allied Dent. Soc., December 2, 1912.

sepsis has developed does one procure cultures of any organism from the blood or the joint fluid. A positive complement deviation, on the other hand, from the blood is a fairly uniform finding. Fever, except in advanced cases of systemic involvement, is not common. Grave anemia of oligochromemic type may be present

FIG. 1



FIG. 2



FIG. 1.—Normal teeth, for comparison. The roots will be seen to blend with the gum, showing no areas between the teeth and gum. The gum fits snugly up to the teeth, all the way up and between the roots. There is, however, in this case an impacted molar which can be seen (to the left of the picture) impinging on its neighbor. This condition may give reflex pain in the ear, neck, etc., and may be mistaken for pus formation (see Case V). It is a favorable location for the development of pus.

FIG. 2.¹⁵—Simple pyorrhea pockets, early stage (left lower first molar).

FIG. 3

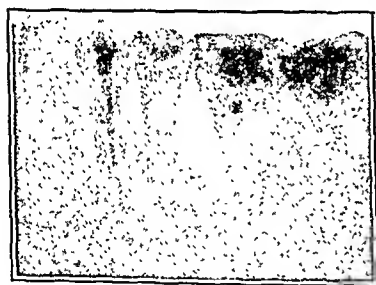


FIG. 4



FIG. 3.¹⁵—Simple pyorrhea pockets; more advanced stage; no involvement elsewhere.

FIG. 4.¹⁵—Typical pyorrhea alveolaris; no involvement of pulp.

in the early stage of dental sepsis. Oligocythemia occurs in cases in which the system has been involved for some time. Grave secondary anemia may develop in such cases. Polynuclear leukocytosis or increase in the number of the white cells is rarely found, even when large pus areas exist in and about the teeth. Glandular enlargement seems to occur more commonly with lower than with

¹⁵ If the general health is not taxed by bad food and bad air, overwork, worry, etc., the condition shown in Figs. 2, 3, and 4 may exist for long periods with or without local manifestation, but usually with moderate systemic disturbance (see Case IV). With the extension of the local process to the tooth or surrounding tissues or with deterioration in health from any cause, the system may become suddenly and seriously involved. (See Case II.)

upper-jaw involvement. The submental and cervical glands are those usually affected.

FIG. 5

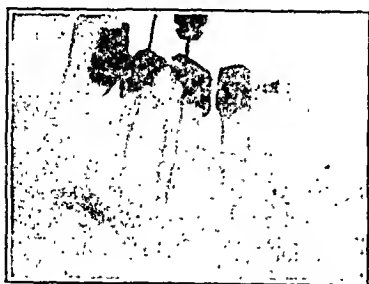


FIG. 6

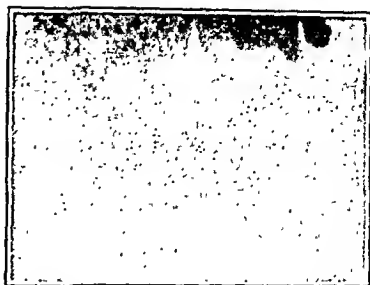


FIG. 5.—Pus in a bifurcation, discharging into the mouth. Destruction of tooth and systemic absorption imminent.

FIG. 6.—Pus pockets with necrosed roots under crowns; systemic absorption active. (See Case II.)

FIG. 7



FIG. 8

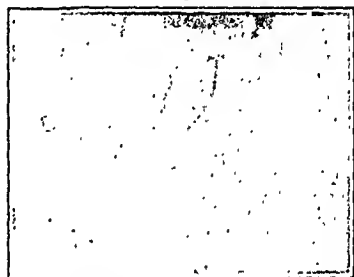


FIG. 7.—Abscesses over bicuspid roots. Advanced stage. Systemic absorption active.

FIG. 8.—Large abscess cavity in lower jaw; considerable loss of bone through septic process.

FIG. 9



FIG. 10



FIG. 9.—Chronic abscess; tooth structure entirely destroyed; tooth floating. No local symptoms, except mobility of tooth and sinking of tooth when patient chewed.

FIG. 10.—Absorption of root by abscess.

DIFFERENTIAL DIAGNOSIS. While the occurrence of pus in and about the teeth has been found to be the cause of serious sepsis in various parts of the system in a large number of cases, the search

for primary foci of pus other than the teeth must be thorough. The deep urethra, the tonsils, the peritonsillar tissues, the antrum,

FIG. 11



FIG. 12



FIG. 11.—Advanced abscess; no signs or symptoms; detected by radiograph only.

FIG. 12.—Chronic abscess.

FIG. 13



FIG. 14

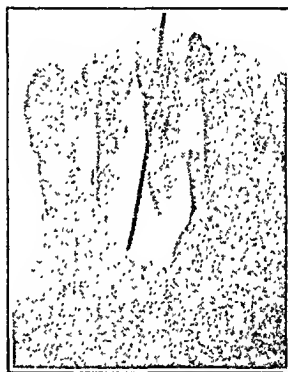


FIG. 13.—Combined Riggs' disease and dental abscess; chronic abscess with fistula; pulp extensively involved.

FIG. 14.—Perforated root; considerable loss of bone.

FIG. 15

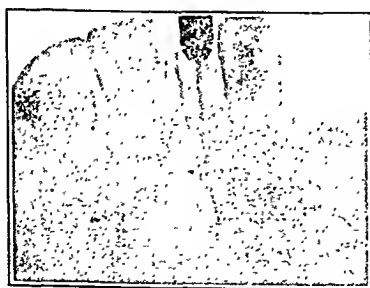


FIG. 15.—Chronic abscess; lateral root; pus draining through canal of pulp; absorption until pus was liberated.

the posterior nares, must all be excluded. The testing out of the blood for complement deviation for various organisms may prove

the most direct evidence in the absence of local manifestation. It may be well to repeat that the blood gives negative cultures unless an advanced degree of sepsis has developed, and in such cases the condition has usually gone beyond the stage in which it can be influenced either by local, general, or vaccine treatment. Case III, while the condition remained localized to one knee, was suspected of being tuberculous. Its real character was detected only when pure cultures of *Streptococcus viridans* from the tooth abscess and a positive complement fixation of the blood for the same organism were obtained, the blood otherwise being negative. Fluid from the knee-joint was also negative.

Radiographs of the teeth should be placed first among the means of detecting pathological conditions in the jaw. In some instances, for example where the pus lies in a thin layer over the tooth and not in sufficient quantity to produce a pocket, nothing may appear on the plate. This occurred in Case I, when by a second examination the pus was reached by probing only.

Reference has already been made to impaction and misplacement, with the consequent swelling and reflex pain which may simulate these septic conditions.

TREATMENT. A realization that one is dealing with abscess cavities, due possibly to the most virulent organisms, with the inevitable absorption of destructive toxins, is essential to the prompt and radical care of these cases. While it is true that the teeth (and possibly the tissues about them) resist the entry of organisms themselves into the system, the possibility of a bacteremia always threatens such cases, with probably the development of new foci of pus in the endocardium and other like vital organs. Abscesses in and about the teeth should be attacked with the same energy as pus foci in any other part of the body. Infected teeth should either be removed entire or in part by operating above the tooth through the gum, an operation now done with great skill by many dental surgeons. Cultures should always be taken *at the time of the removal of the tooth or the operation*, and in the event of a positive culture, vaccines should be prepared and stocked in case they may be needed at some later date. Filling of the teeth and temporizing with a hope of saving a tooth which has been attacked by pus should only be permitted after careful consultation with a competent dentist. The physician is under obligation to the patient to make him realize the seriousness of the possible consequences of the seemingly unimportant condition of the teeth. This part of the treatment cannot be too strongly emphasized, and the responsibility of temporizing with or retaining septic teeth should be placed by the physician and dentist upon the patient.

Through the courtesy of Drs. Vaughan and Tracey, already mentioned, I have the opportunity of showing radiographs illustrating the cases reported here as well as the location and distribution of pus in and about the teeth and gums.

PNEUMONIC HEMIPLEGIAS.

BY CHARLES F. WITHINGTON, M.D.,

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CEREBRAL accidents in pneumonia are not very rare. They may be divided into two classes:

I. Those caused by gross anatomical lesions, such as meningitis of pneumococcic origin, thrombosis, embolism, softening, abscess, etc.

In a recent paper¹ I have shown that among 7600 pneumonic patients there were found 21 cases of pneumococcic meningitis, 4 of embolism, 2 of thrombosis, 1 of softening, 3 of abscess, 2 of edema, 2 of "hemiplegia," 1 of transient aphasia.

II. There remains a second group of hemiplegias to which exclusive attention will be given in this paper. They occur generally in young and rather vigorous people and their prognosis is relatively much better than that of the first group. As many recover, there is in such cases a lack of postmortem evidence to show what lesion, if any, existed.

Four principal explanations of the hemiplegias of this group have been offered.

1. Encephalitis, of the Strümpel type.² Hoppe-Seiler gives pneumonia as one of the rarer causes of encephalitis. The relation of the latter condition to influenza is now generally recognized, and it is possible that it is to pneumonias of influenzal origin that encephalitis has a particular relation. Comby³ has shown that encephalitis is related to other infections, like pertussis, enteritis, mumps, typhoid fever, etc. He says that most of these cases of toxic encephalitis recover and give no chance for being studied by autopsy, but cites a few autopsies in which there "were red discolorations of the cortex, points of hyperemic swelling from congestion and serum, the little vessels engorged with blood, sometimes thrombosed, around them numerous extravasated leukocytes, sometimes the vascular tissues thickened and infiltrated with polynuclear leukocytes; miliary hemorrhages, the neuroglia altered in the whole inflammatory zone; serofibrinous infiltration of the stroma and swelling of the cells, chromatolysis of nerve cells, disappearance of their prolongations, dissociation of nerve fibers, granular bodies," etc. Such cases show clinically a sudden onset in health or in the midst of an infectious disease, convulsions, coma, a "meningitique state," limited paralysis with aphasia or mutism.

¹ Medical and Surgical Reports of the Boston City Hospital, 1913.

² Lehrbuch der Greisenkrankheiten, von Schwalbe, 1909, p. 236.

³ Soc. Méd. des Hôp. de Paris, xxviii, 570 et seq.; also Bull. Méd., 1906, No. 5.

The hemiplegia is usually spasmodic with exaggerated reflexes; Babinski sign. These may be associated with choreic or athetotic movements, tremors like those of disseminated sclerosis, etc. Comby will not admit the diagnosis of meningitis sometimes offered in such cases unless it is confirmed by lumbar puncture.

Leichtenstern⁴ describes cases of primary acute hemorrhagic encephalitis as occurring in various infectious diseases, including ulcerative endocarditis and influenza.

Mollard and Dufourt⁵ in a case of a man taken on the seventh day of pneumonia with marked cerebral symptoms but giving by lumbar puncture a clear fluid and dying the next day, demonstrated an encephalitis. They quote a thesis of Chappet in which the writer was able to show only one case of encephalitis due to pneumonia confirmed by autopsy, but cited several pneumonic hemiplegias followed by recovery in which he believes a large part was played by encephalitis.

Some writers believe this encephalitis may come from a larval meningitis.

Strümpell in the last edition of his *Practice of Medicine* says: "It is of practical importance that according to more recent observations (the author, Oppenheim, and others) a *curable* form of encephalitis also occurs in adults."

Southard⁶ says: "The diagnosis between hemorrhagic encephalitis and cerebral hemorrhage would be impossible on theoretical grounds." He attempts the differentiation between encephalitis and hemorrhage by saying: "Practically the paralyses which characterize hemorrhagic encephalitis do not occur simultaneously with the onset of drowsiness or coma. The signs of some cerebral disease are obvious long before paralyses or convulsions have set in. The paralyses of hemorrhagic encephalitis may increase in intensity from time to time in the course of several hours or a day, presumably owing to the gradual development of inflammatory lesions with oozing of blood."

In the cases of pyogenic encephalitis he finds that the organism concerned is more often the *Staphylococcus pyogenes* than pneumococcus in the ratio of 6 to 2.

2. A second assigned cause of pneumonic hemiplegia is hysteria. This is particularly emphasized in a thesis by Bouulloche, of Paris (1892). Daireaux⁷ is inclined to favor the view at least in some cases.

3. Circulating organisms. If pneumonia is, as is now believed, a septicemia there is little doubt that its organism may be carried in the blood stream to the brain. And as a matter of fact many organisms have been found there. Mollard⁸ says that Pfühl has

⁴ Deutsch. med. Woch., 1892, p. 29.

⁶ Osler's Modern Medicine, vol. vii.

⁸ Loc. cit.

⁵ Lyon Méd., cxvi, 821.

⁷ Arch. gén. de Méd., 1906, p. 2241.

found in the brain the bacillus of Pfeiffer, Kirschman that of Eberth, and Leichtenstern the meningococcus.

Fränkel has investigated the distribution of various organisms in the brain. As to pneumococcus he finds two groups: (a) pure pneumococcus infection; (b) associated pneumococcus infection. But of five cases in which pneumococcus was abundant in the blood, in two the brain was sterile, and in the case of all the organisms the brain was found purer than the blood.

Southard termed certain cases bacterial apoplexy. They all occurred in young people between twelve and twenty-two.

It is a little difficult to understand how circulating organisms should so far mass themselves in the brain as to produce hemiplegia.

4. Circulating toxins. The same objection last mentioned applies to regarding circulating toxins as capable of producing local lesion by direct action.

The role of toxins is more probably an indirect one.

Stephan in 1889 attributed the symptom to a vasomotor ischemia caused by ptomaines in the blood which set up a vascular reflex analogous to what may occur in uremia. There is no anatomical change but the toxic substances when generated in one lung are apt to cause a reflex ischemia in the motor cells of the opposite side. Yet there has been much dispute on which side the paralysis is more likely to occur. Landrieux⁹ says it is on the opposite side from the pneumonia. Daireaux¹⁰ says it is oftenest on the right side.

Aufrecht,¹¹ after describing two cases of pneumonic hemiplegia in children, both of which recovered, suggests that the toxins cause a partial edema of the cerebral substance as a result of the changed constitution of the blood as may occur in uremia.

In his cases the pneumonia was of the upper lobes. He believes that in these cases the negative inspiratory pressure in the mediastinum is most reduced, thereby hindering the reflux of the blood from the cerebrum to the heart and so favoring the escape of serum from the arterial vessels and capillaries into the cerebral substance. But as he believes apex pneumonias are especially rare in children, so he finds such hemiplegias especially rare at that age.

Given, conditions producing cerebral edema, it seems reasonable, as has been suggested by Dr. Robert T. Edes, that hemiplegia might be caused if the posture of the patient made an excess of the fluid gravitate to one side of the brain. It is a matter of common observation how readily an edematous effusion can shift its location, as from the legs to the back. I have found in the Boston City Hospital but one case of marked cerebral edema occurring in pneumonia. This was in the service of Dr. F. H. Williams.

⁹ Rev. gén. de Clin. et de Therap., 1903, xvii, 129.

¹⁰ Loc. cit., 1906, ii, 2241.

¹¹ Archiv f. Kinderheilkunde, Band xi.

A boy, aged eleven months, was said to have had two months previously convulsions and bronchitis. The day of admittance he had eleven convulsions, which are not stated to have been more on one side of the body than on the other. Eight days later he died suddenly. There were found post mortem the last stages of gray hepatization of the left lower lobe, also edema of the brain. Beneath the pia there was a well-marked collection of fluid, the pia being raised above the brain three-eighths of an inch, being more marked on the left side. The brain otherwise was normal. No tuberculosis.

Of the above-mentioned theories of the production of pneumonic hemiplegia it is probable that more than one is correct. We may follow the conclusions of Lesieur and Froment.¹² "The group of pneumonic hemiplegias embraces facts provisionally related to each other, but for which a single pathogeny cannot be shown. Among sources which have been assigned some (theories of congestion and cerebral edema) are founded on trivial lesions whose significance cannot be precisely defined in the absence of histological, chemical, and bacteriological examination. Others (theories of reflex and of hysteria) are rational, but are not as yet well enough demonstrated.

"One must then in various cases attribute pneumonic hemiplegias to ischemia by reason of insufficient cerebral circulation to meningitis, to meningoencephalitis, or to encephalitis.

"It is impossible at present to show with certainty which of these forms of pathogenesis is most frequent."

The phenomenon of pneumonic hemiplegia without gross lesion is not a common one. It appears usually about the second or third day from the onset of the pneumonia. In one case of Aufrecht it preceded the pneumonia by three days. Before the aphasia or paralysis there may be headache, syncope, bewilderment, or vertigo. There may be paresthesia of the side, followed by a frank hemiplegia. The aphasia may come suddenly without impairment of consciousness. "The type of the aphasia is usually ataxic, as in lesions of the third left frontal convolution. The patient can pronounce only a few monosyllables more or less appropriate to what he wishes to say. At first the intellect is blunted and he cannot understand what is said to him, but after a few hours he indicates by gesture that he wishes to talk. There is always a paralysis of the right lower facial, the mouth is drawn to the left, and the tongue deviates to the right. The orbicular is intact. The hemiplegia may be complete, but oftener is limited to the face, tongue, and right upper extremity. The tendon reflex is only slightly affected. To the motor paralysis is often added a *vasomotor*,

¹² Rev. de Méd., October, 1911 (special number in honor of the festival of Lepine).

with redness of the paralyzed area and then a demonstrable increase of temperature."¹³

Again, Lesieur and Froment¹⁴ say: "There is no doubt that a certain number of pneumonic hemiplegias are due to an acute pneumococcic encephalitis. It is equally certain that this must not be considered as the only pathogenesis, to the exclusion of any other."

A good illustration of a typical transient pneumonic aphasia in a young subject is one by Doernberger,¹⁵ which I will briefly condense.

A boy, aged three and a half years, was taken May 9 with coryza followed by bronchitis. Six days later there was lobular consolidation throughout the right lower lobe, on the tenth day the same occurred in the right upper lobe. On the sixteenth day there was consolidation of the left upper and right middle lobes. Temperature, 104.3°. On the same day there was loss of consciousness and of speech; pupils dilated, fixed; occasional scream; otherwise stupid. No response to call. Slight stiffness of neck. No vomiting. Breathing regular, quick, uninterrupted. Patellar reflexes lost; slight stiffness of neck.

On the seventeenth day there were clonic spasms of the left extremities; the face was drawn to the left. These symptoms lessened, and in three days the convulsions and meningeal symptoms had disappeared. On the twenty-sixth day the patient was afebrile; took notice of playthings; made contortions of the face in a vain attempt to speak; pointed to what he wanted and fretted until he obtained it. On the twenty-seventh day of the disease and the eleventh of the aphasia he spoke for the first time, saying yes and no. The speech then returned, at first slow and syllabic, but finally was completely restored.

In this case no lumbar puncture was made to exclude meningitis, but the brevity of the meningeal symptoms and the long continuance of the aphasia indicated that meningitis did not play the chief role.

The mortality of many of these toxic forms of pneumonia with hemiplegia does not seem to be greatly increased by the super-vention of the cerebral symptoms. Some writers, as Moizard¹⁶ and Lesieur¹⁷ have said that most of the cases recover. This statement appears to the writer unduly optimistic. If many recover, the opportunity for postmortem evidence is obviously greatly lessened. But the mortality, so far as it is connected with the general pneumonic septicemia, still remains. So that a few autopsies are on record as bearing on the cerebral pathology.

¹³ Chantemesse, Soc. Méd. des Hôp. de Paris, 1893, x, 875.

¹⁴ Loc. cit.

¹⁵ Jour. de Méd., lxvii, 889.

¹⁷ Soc. Méd. des Hôp. de Paris, xxviii, 570.

¹⁶ Münch. méd. Woch., 1904, li, 833.

One such case is the following which I find in the records of the Boston City Hospital, in the service of a colleague now deceased:

G. C., a negro boy, aged thirteen years, entered the hospital December 27, 1883. The mother said he had "brain fever" when young, but had been well since except for the previous two months, when he had had some headache and had been at times drowsy and forgetful. The present acute illness began four days before he entered the hospital, into which he walked by himself with a temperature of 103.6°.

The symptoms were strongly suggestive of meningitis, and such would have been the diagnosis even after the demonstration of a pneumonia.

He cried out with pain and swallowed with difficulty. He slept most of the time at first. The eyes were turned up and to the right. Pupils were small, responsive, with some lachrymation. He turned mostly to the right side and showed great reluctance at being turned to the left. He moved the left arm and leg much less readily than the right. Tongue protruded to the left; the right side of the mouth was drawn up slightly and the wrinkles were deeper in the right cheek than in the left. Loss of sensation in the left hand and foot, but sensation increased as the hand was passed up the limbs. Hyperæsthetic on the left side of the trunk and face.

Patellar reflex absent on the left side, diminished on the right. Plantar reflex much diminished on the left, possibly slight rigidity of the neck. Short, sharp cries.

The temperature rose from 103° to 104°, and finally just before death rose to 107.5°.

On the sixth day of his disease he was more irritable, and could not bear anyone to touch the bed. There was retraction of the head and stiffness, with flexion of the extremities.

The hemiplegia of the left side was less, though there was still partial paralysis of the left side of the face. The right arm resisted extension. Many rales were noted in both backs, but the diagnosis of pneumonia was apparently not made.

In the following week the stupor and irritability increased, there was clonic spasm of the lower jaw and rigid retraction of the head. Finally, he became noisy and incoherent.

This was before the days of lumbar puncture, and none was used. But what necessary evidence was lacking of a meningitis. The autopsy, however, gave a surprising contradiction to that view. It showed the dura everywhere translucent. While the sinus contained considerable blood, partly in soft coagulation, there was no evidence of thrombosis. The vessels of the base and the fissure of Sylvius were normal.

The pia everywhere was thin and delicate; its meshes contained a little clear fluid. The lateral ventricles had only enough fluid

to moisten their surfaces. The ependyma everywhere was smooth and shining. The brain substance was in general firm, the gray cortex of the usual thickness and "of a dark purplish tint." No tubercles were present. The white matter was of good color, with abundant puncta cruenta. The cord and its membrane were normal.

The lungs showed a chronic adhesive pleurisy, with an acute process on the right pleura, a diffuse purulent bronchitis and an extensive bronchopneumonia of both lungs.

Unless the purplish color of the gray matter and the abundant puncta cruenta of the white may be taken to indicate a slight degree of encephalitis, there was nothing in the section of the brain to explain the marked cerebral symptoms. The death was from the pneumonia, and the brain condition, which of and by itself would doubtless have been recovered from, seemed to have been wholly a toxic affair.

With the foregoing case compare one of Balzer, quoted by Chantemesse,¹⁸ where a patient with aphasia died five days later of pneumonia. The brain was perfectly normal and microscopic examination of the third frontal convolution showed *nil*.

The following case, which I found in the records of Dr. T. M. Rotch, is a rather better marked one of encephalitis, but it gave no such localized symptoms as did the last one, and the patient died without showing any hemiplegia. It seems to support the view of Comby that encephalitis may be associated with pneumococcus meningitis:

A young Italian man, aged twenty-two years, had been sick two weeks, with a history of fever, cough, and bloody sputum. On entrance there were signs of pneumonia in the right back. The patient made rotary motions with his arms and had frequent muscular twitchings. There was neither paralysis nor strabismus. He became unconscious and died the next day.

The autopsy showed a marked meningitis, involving convexity and base, with pus about the vessels, especially in the commissures and the fissure of Sylvius.

Besides this it was noted that in the right lateral ventricles there were several minute red spots beneath the ependyma representing small extravasations of blood. The whole brain was injected, the puncta cruenta marked. The general color of the brain substance was of a pinkish tint.

The following case illustrates a transient aphasia in the course of pneumonia without other paralysis and resulting in complete recovery:

The patient, Edith V., a married woman, aged thirty-one years, had been subject to what were evidently attacks of epilepsy occur-

¹⁸ Loc. cit.

ring every month. She is said to have been in an insane asylum a year ago. Five days before the present illness she had such an attack and fell to the floor, but quickly recovered and returned to work. There was no specific or alcoholic history. The following day she stayed in bed on account of abdominal pain and general weakness.

She entered the hospital April 8, 1906, with a temperature of 104°. Leukocytosis, 22,500. Consolidation of the right lower back. The next day the speech became unintelligible. Loss of control of bladder and rectum, but no hemiplegia. Consciousness intact. Four days later the speech was somewhat clearer, but still ataxic aphasia. Two days later the consolidation had increased in the right lung and was present in the left. Five days later it was noted that some words were still imperfectly pronounced, but that she did better on a second attempt. She wrote well and read aloud better than she talked. The tongue protruded slightly to the right; movements of face and of extremities were normal. Pupils were equal and eye motions were normal. Knee-jerks were equal and normal.

Four days later, fifteen days after admission and fourteen after the aphasia, she was talking much better, and the lungs were clear. She was up and about and was discharged well.

The most remarkable case which has come under the observation of the writer, of grave cerebral symptoms occurring consecutively to pneumonia and apparently presaging a fatal result, is the following, which was seen in consultation at the Boston State (Insane) Hospital. I have included it in the paper already referred to in the *Medical and Surgical Reports of the Boston City Hospital*, 1913.¹⁹

The patient, W. M., aged twenty-seven years, was an attendant in that institution and a strong and healthy man of admirable habits.

On February 5, 1912, the patient complained to his friends of headache and general pains. On February 7 he was off duty and went to bed, complaining of headache and general pains in the shoulders, back, and legs. Constipated. Temperature, 100°. On February 10 his temperature was 104°, and he complained of a slight pain in his chest. No sign of pneumonia was found. He also had a little cough without expectoration. For the next six days his temperature was irregular, between normal and 101°. On February 16 he had a perfectly normal temperature and said that he was feeling much better, so that the physician did not see him at all on February 17. On the morning of February 18 he complained of headache and appeared rather dull, answering questions mostly with yes or no. Still no signs of pneumonia were

¹⁹ Also Boston Medical and Surgical Journal, June, 26, 1913.

found. When seen at 3 P.M. he showed partial aphasia and partial paralysis of the muscles of the right side of the face, but he was then able to walk, and assisted himself while being moved to another room. At 8 P.M. he had complete aphasia and diminished grip in the right hand, but he could move both the right arm and leg and turn over in bed when asked to do so. He understood all that was said to him and coöperated readily with the exception of talking. His temperature at 6 P.M. was 102.4° . At 10.30 P.M. he had a severe attack of propulsive vomiting. I was asked to see the patient on February 19, when, after getting the foregoing history, the following condition was observed: The patient was dull, saying nothing. He protruded his tongue when requested. Pupils were equal and responsive. No oculomotor paralysis. Right side of the face did not move; right arm was fully paralyzed except for slight movement of the fingers; paralysis of the right leg was nearly complete. Sensation was absent on paralyzed side. Complete aphasia. Knee-jerks were equal and normal. Incontinent. Babinski reaction and ankle clonus on right side. Oppenheim and Mendel reaction on right side. The heart sounds were clear and there was slight dulness outside the heart apex. No abnormal auscultatory sounds were heard. Respiration was shallow and the patient could not be made to cough or to take a long breath. In view of the septic temperature and the sudden nearly complete paralysis with its reflex anomalies noted, in a young and previously healthy man, the opinion was expressed that he probably had a septic thrombosis, the infection originating in the chest. The blood count which on February 18 showed 19,600, was 13,200, with 93 per cent. of polymorphonuclears. Lumbar puncture brought a clear fluid, which was later reported sterile. Widal reaction was negative. Blood culture was also later reported as negative.

February 20. Temperature at 6 A.M. was 102.2° and at 6 P.M. the same. He voided urine and feces in bed, and while he followed the nurses and physician with his eyes, he evidently did not know what was transpiring. However, if asked if his head ached and where it ached, he rubbed his hand over the right side of his head.

Two days later (February 22) I saw him again. The morning temperature was then 104.6° . Pulse, 92. Respiration, 46. The paralysis of the right side was complete. Pain sense absent. No paralysis on the left side. He was able to swallow, but with difficulty, and the attempt caused coughing and choking. Said nothing and apparently did not recognize his sister, who had arrived from a distance. In the left back, in which the dulness was found two days before, there were fine rales over limited areas, warranting the diagnosis of bronchopneumonia. The prognosis, in view of the more cerebral condition, was considered highly unfavorable. The event, however, contradicted this prognosis, for after five days of desperate illness the temperature fell and improvement began,

For the remaining as well as the earlier history I am indebted to the careful record of Dr. E. C. Noble, who was in charge of the case.

For the next three or four days the temperature remained elevated, but in two days he swallowed a little better. On the morning of February 26 the temperature dropped to 99°. He still was incontinent and very restless; aphasia and paralysis complete. Two days later he appeared to recognize the physician and his friends and slightly moved the fingers of the right hand. No other movement of paralyzed side. Babinski and clonus were present on the right side. Knee-jerks were equal.

March 1, A.M. He slightly moved the right arm but not the foot. In the afternoon he could flex the arm and move the foot a trifle.

March 3. He spoke for the first time at 7 o'clock. This was only a muffled sound in reply to someone saying good morning. He said nothing more until 10 P.M., when he distinctly asked, "What time is it?" Temperature normal; still incontinent of urine.

March 4. No longer incontinent. Speech thick. No attempt made to make him talk, but he said a few words with effort and seemed pleased at doing so.

March 10. Speech returned, also motions of right side. A slight Babinski and very slight ankle clonus remained.

March 20. Steady improvement during the last ten days. Temperature normal; eating well. Moved unaided from bed to chair. Dressed for first time.

April 1. Walked outdoors for last seven days and started for Vermont. No paralysis, aphasia, Babinski, nor clonus. Patellar reflexes equal and normal.

The importance of the phenomena previously discussed is great from the prognostic point of view and seems to be hardly appreciated.

The diagnosis is sometimes difficult, especially from cases of meningitis. Lumbar puncture should always be made to assist the diagnosis. The fluid in meningitis is turbid, and may show culturally or by inoculation the pneumococcus, or if the meningococcus, it manifestly removes the case from the category we have been considering. Polynuclear leukocytes predominate in bacterial meningitides and lymphocytes in granular ones. In encephalitis there is no leukocytosis, and the fluid is clear.

It may be said in passing that the statement of Hoppe-Seiler, Moizard, and others that the prognosis of pneumococcus meningitis is unqualifiedly bad is not absolutely true, as Holt²⁰ has reported a case in which, though the pneumococcus was demonstrated in the fluid removed by lumbar puncture, the patient recovered.

It should also be borne in mind from the point of view of the diagnosis of meningitis that the latter disease may exist especially in alcoholic patients without symptoms. Hoppe-Seiler²¹ says that it may occur in old men without stiffness of the neck, vomiting, or motor irritation. In drinkers symptoms may be ascribed to delirium tremens, which are really due to a purulent pneumococcic meningitis of the convexity.

In proportion as one can be sure in his exclusion of the organic group of hemiplegias the prognosis is relatively favorable. We still have the pneumonia to reckon with. But if it is true that the cerebral accident does not materially add to the gravity of the pneumonia, one is justified, on the whole, in giving a rather favorable prognosis to such cases, occurring, as they generally do in young and strong subjects.

SPLENECTOMY FOR SPLENOMEGALY (GAUCHER TYPE).

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THIS rare type of splenic affection of undetermined etiology received its name following the publication of the doctorate thesis of P. C. E. Gaucher in Paris, 1882, under the title "*De l'Epitelioma Primitif de la Rate; Hypertrophie Idiopathique de la Rate Sans Leucemie.*"¹ Following this, in 1895, Collier² published the second case, and in 1896, Picou and Ramond³ published a case previously reported by the former the year preceding. Bovaird⁴ published the initial American case in 1900, this being the fourth on record. The first mention of the condition in German literature was made by Schlagenhauser in 1907.⁵ To date there are sixteen cases recorded in which the clinical diagnosis has been confirmed by operation or autopsy, that of Truelson⁶ not being included in the list, because the operative or histological findings do not seem determinative and because no autopsy was performed after the so-called "recurrence."

The earliest recorded splenectomy for this condition (1895) is the case of Picou and Ramond³ in a patient aged thirty-two years, operated upon for suspected uterine fibroid.

The second splenectomy for authenticated splenomegaly (Gaucher) was a girl, aged thirteen years, operated upon May 17, 1899, by the late A. J. McCosh at the request of Bovaird.⁴

The third case was operated upon in 1905 and is mentioned in an article by von Herczel⁷ in 1907, the true nature of the condition not being determined until that time.

Wilson¹² reports the fourth and fifth cases (1907 and 1908) from the Mayo clinic, these having been previously reported as examples of chronic hyperplasia,³³ as stated by Downes in his recent article.¹⁴

De Jong and Van Heukelom⁸ report the sixth case, 1910. In this case the liver continued to enlarge after the splenectomy, and the authors ascribe this to the proliferation of the cells carried there previously from the spleen.

The seventh case (1911) is reported from the Mayo clinic, by Wilson,¹² and this is the first successful American case with an initial pathological diagnosis.

The eighth case was first reported by Reuben⁹ in January, 1912, and the operative and autopsy findings (March, 1912) are recorded by Mandelbaum.¹⁰

The ninth case is reported by Downes,¹⁴ April, 1913.

The tenth case is herewith reported, and in point of age it is the youngest on record. The other case mentioned by us as occurring in the same family was doubtless of the same type, but it is unincorporated in the lists because there was no operative or pathological verification.

It is significant that of the ten recorded operative cases there is a family history of the condition in five: Bovaird's, Von Herczel's, De Jong and Van Heukelom's, Reuben and Mandelbaum's, Erdmann and Moorhead's.

Weichselbaum¹¹ in 1881 reports a splenectomy in a twenty-one year-old soldier; no history is given, but the statement is made that the spleen was enlarged and the title of the article would indicate that the organ was of the Gaucher type. This case is not fully authenticated, and therefore is not recorded with the foregoing.

A tabulation of the recorded cases in the literature has been made by Reuben,⁹ and Mandelbaum's¹¹ and Wilson's¹² recent articles contain a valuable pathological digest of the cases regarded by them as authentic.

The literature now contains some sixteen cases verified by operative or autopsy findings.

The following is a list of the cases submitted to operation:

Priority of publication.	Author and date of publication.	Sex and age.	Blood picture.	Operator and date of operation.	Weight and size.	Outcome.	Duration of enlargement.	Other cases in family.	Priority of operation.
1	Picou and Ramond 1896	Female 32 yrs.	Simple anemia	? 1895	2800 gm.	R.	?	?	1
2	Bovaird 1900	Female 16 yrs.	Simple anemia	McCosh May 17	12½ lbs.	Died in 3 hrs	13 yrs.	Yes	2
3	v. Herczel 1907	Female 37 yrs.	Simple anemia	v. Herczel Sept. 27 1905	3 kg. 32x16 x12 cm.	R.	4 yrs.	Yes	3
4	de Jong and von Heukelom 1910	Female 12½ yrs.	Simple anemia	von Rossem March 29 1909	1850 gm. 26x15 x7 cm.	R.	6½ yrs.	Yes	6
5	Maudelbaum 1912	Male 4½ yrs.	Simple anemia	Wiener March 1 1912	490 gm. 18x9.5 x5 cm.	Died next day	1 yr.	Yes	8
6	Wilson* 1913	Female 27 yrs.	Simple anemia	W. J. Mayo Jan. 7 1907	5280 gm.	R.	?	?	4
7	Wilson* 1913	Female 37 yrs.	Simple anemia	W. J. Mayo May 11 1908	895 gm.	R.	?	?	5
8	Wilson 1913	Female 25 yrs.	Simple anemia	W. J. Mayo Sept. 26 1911	4500 gm.	R.	?	?	7
9	Downes 1913	Female 28 yrs.	Simple anemia	Downes Dec. 14 1912	1813 gm. 35x13.5 x6.5 cm.	R.	15 yrs.	No	10
10	Erdmann and Moorhead 1913	Female 3¼ yrs.	Simple anemia	Erdmann June 6 1912	430 gm. 17x10.5 x7 cm.	R.	2 yrs.	Yes	9

* These cases are not as yet fully authenticated.

SUMMARY.

Female, 9; male, 1.

Recovered, 8; died, 2.

Oldest, 37; youngest, 3.

Other cases in family, 5; unstated, 4; none, 1.

Longest duration, fifteen years; shortest, one year.

The clinical aspects of the affection have been well described by numerous authors, notably Bovaird,⁴ Brill, Mandelbaum, Libmann,¹¹ Reuben,⁹ and best and most recently from a critical pathological standpoint by Mandelbaum.¹⁰ For this reason, and because the diagnosis is relatively plain, we purposely refrain from discussing the medical or clinical features, and revert to the propriety of splenectomy as the treatment of choice, in effect regarding the condition as an operable tumor of the spleen. We are led to advocate operation for the following reasons:

1. All known forms of therapy have hitherto failed, including x-ray treatment.

2. Even in advanced cases splenectomy has resulted in relief of symptoms (weight, pressure, gastric and intestinal distress, malnutrition, etc).

3. Removal of the organ is regarded as the method of choice in Banti's disease and splenic anemia, many splenectomies for these and allied conditions now being recorded; hence the analogy seems warranted.

4. The hemogenetic (or ferrogenetic) function of the spleen is apparently unaffected after splenectomy, as indicated by a prompt return of the blood to normal.

5. Early recognition of suitable cases should result in a low operative mortality, as the operation *per se* in this class is not much more hazardous than for other intra-abdominal neoplasms.

Carsten¹⁵ reports a mortality of 18.5 per cent. in a collection of 739 cases of splenectomy for various lesions.

Johnson¹⁶ reports a mortality of 27.4 per cent. in 708 collected cases. These statistics indicate an average operative mortality of about 23 per cent., which seems abnormally high.

W. J. Mayo¹³ reports 27 splenectomies (3 of Gaucher ? type), with 2 operative deaths. Of this number 12 remained well one to seven years; 6 were well less than two and a half years. He is of the opinion that the mortality should not exceed 10 per cent.

Wilson,¹² in reporting the pathology of the splenic material from the Mayo clinic, states: "It seems to me unfortunate that the trend of medical thought was originally directed toward the consideration of these endothelial proliferations as true neoplasms, with the associated dread of malignancy, since it has no doubt operated to prevent surgeons from hazarding splenectomy; of the 9 cases which have been operated on, as reported in the literature, 4 have recovered, while the remaining 5 were in a bad condition before coming to operation." Inferentially he intimates that operative interference is as much indicated for splenic connective-tissue overgrowth as for similar pathological changes in the thyroid and prostate.

"Further, the survey of all the (Gaucher) cases suggests a close analogy in their histology with what one meets with in hyperplasias of the thyroid and of the prostate, namely, an initial hyperplasia of the parenchyma filling the acini, a secondary increase of the stroma, and ultimately a degeneration of the parenchyma, with contraction of the connective-tissue."

It appears that ligation of the bloodvessels for various forms of splenomegaly has been practised, but that the mortality is high is indicated by the remark of D. A. K. Steele, who stated that of six cases thus operated upon, four died (discussion of Harris and Herzog's paper).²⁴

Cases of enlarged spleen showing a practically normal blood-picture, with a hemoglobin percentage of fifty or more, offer the

best prospects for operative interference. Associated pigmentation or marked enlargement of the liver or glands are not contra-indications if the general condition of the patient is good.

Operative complications are generally in the nature of adhesions (intestinal, gastric, pancreatic, parietal, diaphragmatic), adventitious or friable bloodvessels, and attendant shock from manipulation or hemorrhage.

Operative shock and hemorrhage are guarded against by a reasonably large incision and a minimum of intra-abdominal trauma especially to the diaphragm. In motile spleens, primary clamping of the main bloodvessels should be the first step; in other cases, division of the adhesions between clamps is the initial procedure, unless immediate ligation can be more speedily performed. When the organ is large, the bodily blood-supply depleted, or hemorrhage is anticipated, it may be expedient to first expose a vein at the bend of the elbow so that a saline intravenous infusion may be given if necessary. Normally the weight of the spleen in a twelve year-old child is $\frac{1}{400}$ of the body weight; obviously, in a much enlarged spleen, the removal of the organ and the contained blood will cause much depletion, and this can best be counteracted by saline intravenous infusion. Postoperative fever occasionally occurs independent of infection, but ordinarily no special treatment for this is required. It is often easier to deliver the organ from below than from above, and separate ligation of the individual vessels is advisable when practicable.

In the two cases herewith reported it may be stated that the parents are robust and of a highly developed mental and physical type; American born; no constitutional dyscrasiæ.

A genealogical search extending over five generations shows that most of the forebears lived sixty years or more.

The oldest child, Henry, was born March 21, 1901; said to have been an eleven months' pregnancy. Weight, 7 pounds at birth; breast-fed until tenth month. Weight at five months, 13 pounds 10 ounces. Weight at one year, 18 pounds 4 ounces.

Abdominal protrusion first noted about July 2, 1902, and at that time spleen and liver were found enlarged by the family physician, Dr. W. C. Walser, of Staten Island. Blood examination then disclosed malarial parasites, and under appropriate treatment the child seemed to improve.

January 15, 1903. Blood-count (by Dr. H. W. Patterson) showed:

Hemoglobin	62 per cent.
Red blood cells	3,912,000
White blood cells	4,600
Small mononuclears	12.5 per cent.
Large mononuclears	20.0 "
Polynuclears	50.0 "
Basophiles	6.0 "
Eosinophiles	12.5 "

January 22, 1903. Seen by a consultant, who had blood-examination made, which showed a picture similar to the foregoing. A chronic colitis now existed in addition to the splenic and hepatic enlargement.

October 20, 1904. Seen by two other consultants. Various remedies were being constantly administered.

September 18, 1906. Blood-examination by Dr. James Ewing, at request of another consultant, showed practically no changes from the preceding, and a tentative diagnosis of splenic anemia or simple splenomegaly was made.

November 20, 1906. Seen by a former consultant, who stated that the liver and spleen had decreased since the examination of October, 1904.

November 26, 1906. Seen by another consultant, who diagnosed splenomegaly.

January 1, 1907. Developed pneumonia, with low temperature and much prostration, the cough lasting all spring.

October 27, 1907. Died of pneumonia after one day's illness. No autopsy.

At no time were there any hemorrhages, except slight epistaxis. On one occasion in the latter months "he vomited a great deal, and often looked dark and blackened."

The second child, Frederick, was born February 7, 1903, and is exceptionally strong and well. At the present time he shows no evidences of enlarged spleen or liver.

The third child, William, was born May 8, 1907, and is in splendid health now; no splenic or hepatic involvement.

The fourth child, Elizabeth, is our patient. She was born February 19, 1909; normal delivery; weight at birth, $7\frac{1}{2}$ pounds. Breast-fed until seventh month, and then weighed 14 pounds 10 ounces.

November 27, 1909. Had bronchitis; sick for ten days. Weighed 18 pounds at end of first year.

April 8, 1910. Spleen was found slightly enlarged, and at this time a blood-examination was made at the request of Dr. W. C. Walser, of Staten Island, by Dr. H. W. Patterson, and it showed:

Hemoglobin	70 per cent.
Red blood cells	2,956,000
White blood cells	14,000
Small mononuclears	13.0 per cent.
Large mononuclears	28.6 "
Polynuclears	41.0 "
Eosinophiles	2.0 "
Basophiles	2.0 "
Myelocytes	12.3 "
Transitionals	1.0 "

At this time she seemed "rather nervous and hard to nourish, the only illness was slight colds."

February 1, 1911. Second blood-count at Dr. Walser's request by Dr. Patterson:

Hemoglobin	83 per cent.
Red blood cells	6,104,000
White blood cells	10,800
Small mononuclears	30.0 per cent.
Large mononuclears	19.0 "
Polynuclears	47.0 "
Eosinophiles	1.0 "
Basophiles	1.0 "
Transitionals	2.0 "

May 27, 1911. Feet badly burned in hot sand, and she was quite ill for several weeks. At this time Dr. Walser noted a considerable increase in the size of the spleen; liver normal.

In July, 1911, she was examined by Dr. R. H. Van Denburg, of Cossackie, New York, and the splenic enlargement was still present, but the liver was normal. He again saw her September 23, 1911, and found the liver enlarged.

January 24, 1912. Blood-examination showed no special changes from the preceding.

February 21, 1912. Seen by a consultant, and the blood-examination then disclosed:

Hemoglobin (Sahli)	56 per cent.
Red blood cells	5,000,000
White blood cells	9800
Polynuclears	45.0 per cent.
Lymphocytes	55.0 per cent.

Wassermann negative.

At that time the spleen reached to the umbilicus; the liver was smooth, thin edged, and moderately enlarged; no ascites; abdominal veins were enlarged; inguinal glands were enlarged, all others were normal. Splenectomy was suggested if the surgeon justified the risk involved.

February 28, 1912. Blood-examination by Dr. F. E. Sondern at the request of the writers:

Hemoglobin	85 per cent.
Red blood cells (small, varied, and pale)	6,200,000
White blood cells	7000
Small lymphocytes	49.4 per cent.
Large lymphocytes	9.4 "
Polynuclears	40.0 "
Eosinophiles	1.0 "
Basophilcs	0.2 "

No malarial plasmodia.

Wassermann negative.

March 2, 1912. Examination by the writers showed a rather pale, poorly developed, somewhat dyspneic child of three years

of age. The abdomen was uniformly protuberant and the overlying veins were prominent. No ascites. Liver was smooth, firm, and non-tender, reaching about two inches beneath the costal margin and extending well to the left. Spleen was firm, smooth, non-tender, and reached just below the umbilicus and well toward the median line (Fig. 1). There was one enlarged lymph node in the right inguinal region. No jaundice nor pigmentation. Sclera clear. Bones normal.

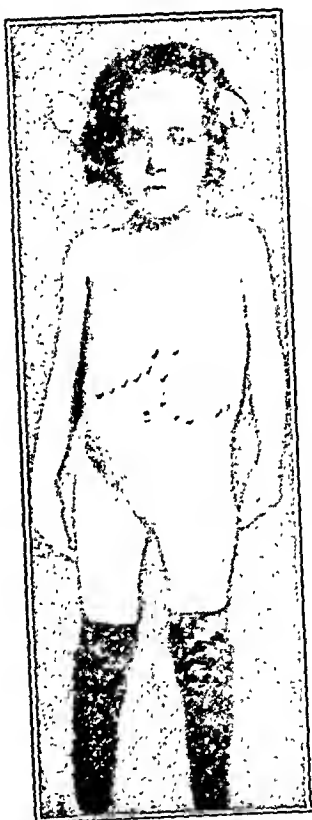


FIG. 1.—Original level of liver and spleen.



FIG. 2.—Present level of liver and operative scar.

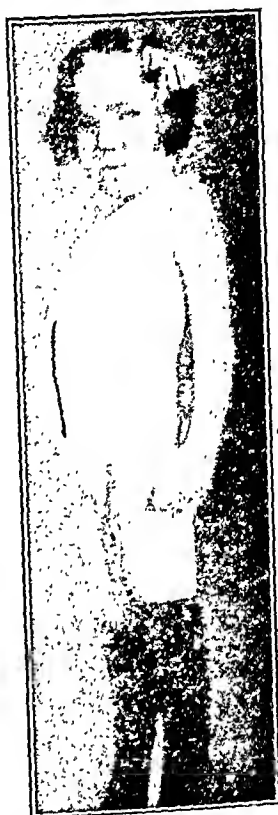


FIG. 3.—Abdominal protrusion and operative scar.

Splenectomy was advised in view of the fatal outcome of the other case in the same family, the apparent progressive loss of strength, and because no improvement had occurred despite varied sustained medication. The operation was postponed because of a severe attack of bronchitis accompanied by mastoiditis. Weight just before operation, $26\frac{1}{4}$ pounds.

June 6, 1912. Splenectomy by Dr. John F. Erdmann assisted by Drs. Moorhead and Russell. Gas-ether anesthesia by Dr. Bennett.

The abdomen was entered through a long incision at the outer border of the left rectus muscle. The spleen was found relatively

free, the main attachment being to the splenic flexure and pancreas, and in freeing it from the latter a small portion of the tail of the pancreas was purposely exsected. The splenic vessels were secured by clamps and the organ removed. Separate iodine catgut ligatures for the vessels. Tier sutures of iodine catgut for peritoneum, muscle, and rectus sheath. Continuous lock-stitch suture of the skin. Time of operation, twenty-seven minutes. There was never any temperature over 100°. The patient made a perfect recovery, and left the hospital in two weeks, then weighing 24½ pounds.

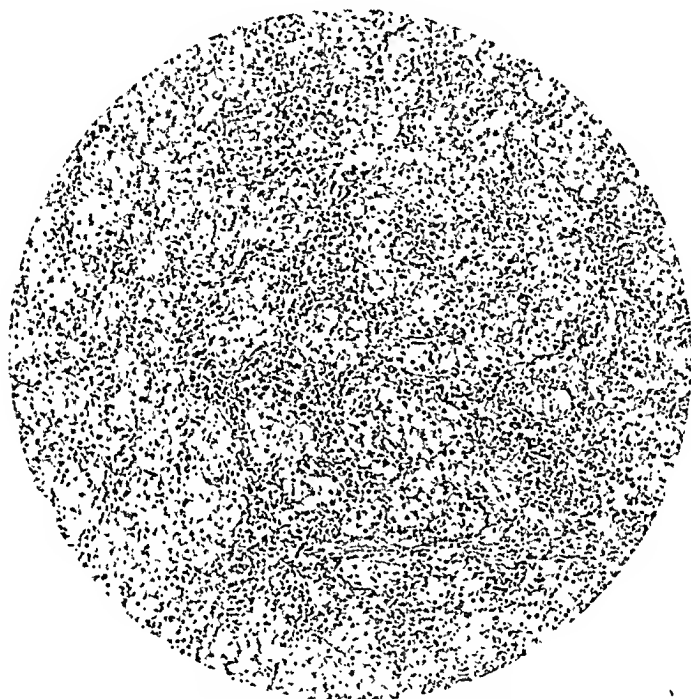


FIG. 4.—Section of spleen showing alveoli filled with large cells. Dr. Sondern.

Following is the histological examination as reported by Dr. F. E. Sondern:

The striking lesion microscopically in the spleen is the presence of enormous numbers of large mononuclear cells. These cells are arranged in alveoli throughout the organ, outlined in an irregular manner by a relatively scant connective-tissue network. The nuclei of the cells, which readily stain, are usually centrally situated, but often eccentrically, and occasionally at the border of the cell. The protoplasm is granular and stains faintly. A few of the cells contain vacuoles. Very rarely a cell with two or three nuclei is seen. Connective-tissue fibrils are not apparent between the cells except at the edges of the alveoli, where the cells lie adjacent to the connective tissue.

The endothelium of the venous sinuses is swollen, and occasionally large cells are seen within the lumina, apparently of the same type as those seen elsewhere throughout the pulp.

The Malpighian bodies are few and not increased in size. Scattered among the lymphoid cells of the follicles are a few of appar-

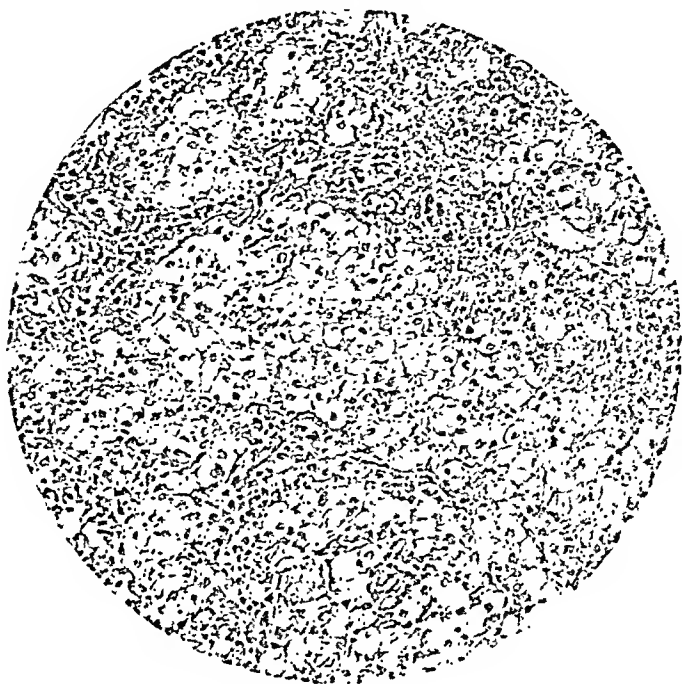


FIG. 5.—Section of spleen showing alveoli filled with large cells. Dr. Sondern. $\times 500$.

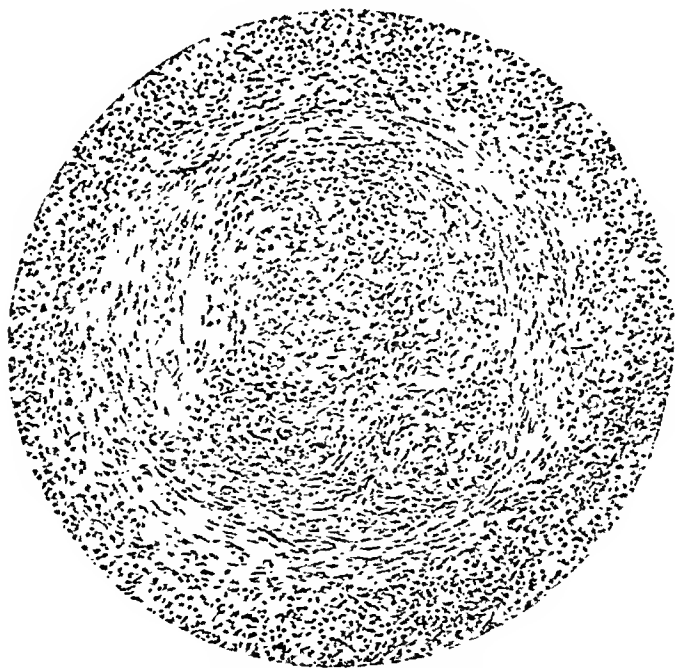


FIG. 6.—Tubercles in spleen. Dr. Mandelbaum

ently the same large mononuclear cells. There are no areas of degeneration or necrosis.

Sections were also made and studied by Dr. F. S. Mandelbaum, who found typical tubercles in addition.

The lesion is a primary splenomegaly of the type first described by Gaucher. It is difficult to determine absolutely the nature of the cells making up the bulk of the tissue. From the morphological appearance of the cells and the swollen condition of the endothelium of the small vessels they are believed to be of endothelial origin.

Spreads made from the surface of the spleen show rather small and pale red cells. There are relatively few leukocytes, with differential count as follows:

Small lymphocytes	74.2 per cent.
Large lymphocytes	7.2 "
Polynuclears	15.6 "
Eosinophiles	3.0 "
Basophiles	none

June 15, 1912 (nine days postoperative). Blood examination by Dr. Sondern shows:

Hemoglobin	85 per cent.
Red blood cells	6,080,000
White blood cells	19,000
Small lymphocytes	24.4 per cent.
Large lymphocytes	20.4 "
Polynuclears	52.6 "
Eosinophiles	2.2 "
Basophiles	0.4 "

July 8, 1912 (one month postoperative). Blood-examination by Dr. Sondern:

Hemoglobin	78 per cent.
Red blood cells	5,200,000
White blood cells	12,000
Small lymphocytes	32.4 per cent.
Large lymphocytes	12.0 "
Polynuclears	53.2 "
Eosinophiles	2.0 "
Basophiles	4.0 "

During the summer the child was reported as being much stronger, and far more active than ever before.

September 28, 1912. Examination by one of us showed her to be apparently in good health, the improvement in color being quite noticeable. The protrusion of the abdomen is less marked; no dyspnea; no dilatation of the surface veins; scar firm. Periumbilical circumference, seventeen and three-fourths inches. Liver reaches about one inch below costal border. No inguinal adenitis.

Weight, 26 pounds. Appetite reported as being enormous (Figs. 2 and 3).

March 2, 1913. Reëxamination shows the general appearance to be good. Liver apparently slightly larger than at the previous examination. Peri-umbilical circumference, twenty inches. She is active, strong, and apparently in perfect health.

April 22, 1913 (ten and a half months postoperative). Blood-examination by Dr. Sondern:

Hemoglobin	75 per cent.
Red blood cells	5,300,000
White blood cells	16,000
Small lymphocytes	47.2 per cent.
Large lymphocytes	8.2 "
Polynuclears	43.0 "
Eosinophiles	1.2 "
Basophiles	0.4 "

NOTE.—October 6, 1913 (sixteen months post operative) the child is reported as well and strong.

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THE SUPPOSED RELATION BETWEEN PARALYSIS AGITANS AND INSUFFICIENCY OF THE PARATHYROID GLANDS.

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LUNDBERG¹ in 1904 and Berkeley² in 1905 suggested that parathyroid insufficiency may be responsible for the symptoms of paralysis agitans. That these symptoms in many ways resemble those observed after removal of the parathyroids in lower animals is true, but attempts at establishing a close relationship between the two have not been successful. Examination of the parathyroids removed from cases of paralysis agitans at autopsy has revealed no characteristic deviation from the normal.³ Berkeley⁴ lays great stress upon the results he has obtained in the treatment of paralysis agitans with parathyroid preparations. Others,⁵ however, have not observed favorable results from such treatment. Roussy and Clunet,⁶ indeed, claim that the administration of parathyroid to their patients increased the severity of the symptoms. They also report finding hyperplastic parathyroids at autopsy, and come to the conclusion that hypertrophy of the parathyroid is an important factor in the etiology of paralysis agitans. This view is exactly contrary to that of Lundberg and Berkeley.

It seemed desirable to attack the subject from another direction, indicated by the results of the author's experiments upon dogs.⁷ These have shown that after parathyroidectomy there is a marked diminution in the excretion of phosphorus. This persists until tetany appears and even longer. Analyses of the blood and serum of parathyroidectomized dogs show a decided increase in the content of phosphorus above the normal. This is due almost entirely to an increase in those phosphorus compounds that are not soluble in acetone, alcohol, or ether, but which are soluble in a mixture of dilute hydrochloric or acetic acid, and picric acid. This increase can readily be demonstrated before marked tetany has developed.

¹ *Deut. Zeitschr. f. Nervenheilkunde*, 1904, xxvii, p. 217.

² *Med. News*, 1905, lxxvii, p. 1060.

³ Thompson, *Jour. Med. Res.*, 1906, x, p. 399; Erdheim, *Mitt. Grenz. d. Med. u. Chir.* 1906, xvi, p. 731; Berkeley, *Presbyterian Hospital Reports*, 1906, p. 170; *Camp. Jour. Amer. Med. Assoc.*, 1907, xlviii, p. 1230; Alquier, *Gaz. des Hôp.*, 1909, lxxxii, p. 1653; Gjestland, *Zeitschr. klin. Med.*, 1912, lxxvi, p. 237; Haberfeld, Marañon, cited in Biedl, *Inn. Sekretion*, 1913, 2d. ed., p. 107.

⁴ *Internat. Clinics*, 1912, series 22, vol. iv.

⁵ Parhon and Golstein, *Les Sécrétions internes*, 1909, cited by Morel, *Les Parathyroides*, 1912, p. 292.

⁶ *Arch. méd. exp.*, 1910, xxii, p. 462.

⁷ Greenwald, *Amer. Jour. Physiol.*, 1911, xxviii, p. 103; *Jour. Biol. Chem.*, 1913, xiv, pp. 363 and 369.

If parathyroid insufficiency is a factor in the etiology of paralysis agitans, it is probable that a similar increase in the amount of acid-soluble phosphorus would be found in the blood-serum of patients with paralysis agitans. It was therefore determined to apply the above test to the study of human serum. Since data concerning the lipid-phosphorus content of human serum are not very extensive, this was also estimated. The results are therefore included in the table, although they are not relevant to the question under discussion.

The patients were selected by Dr. S. Wachsmann, medical director of the Montefiore Home, and the blood was drawn by Dr. H. Smith, to both of whom I am greatly indebted for their cooperation.

On the morning the blood was to be taken the patients received no food. In this way variations due to the character of the food and the stage of absorption were avoided. At about ten o'clock, or sixteen hours after the last meal, the blood was drawn from one of the veins of the forearm into sterile test-tubes and allowed to clot. The next day the serum was poured off and freed of cells by centrifuging. The absolutely clear and hemoglobin-free serum, generally about 50 gm., was weighed in a 700 c.c. Erlenmeyer flask and treated with at least four times its weight of acetone. This served to precipitate all the protein and the inorganic phosphate, leaving only the lipid phosphorus in solution. It is important that the serum be clear and free from hemoglobin, as otherwise it contains enough inorganic phosphate derived from the erythrocytes to vitiate the analyses.

After standing at least six hours the mixture was poured into a wide glass tube, on the lower end of which was tied a piece of fine linen cloth, which acted as a filter. The filtrate was collected in a flask. The precipitate was rinsed into the tube with acetone and allowed to drain for several hours. It was then extracted with hot acetone in a continuous extraction apparatus for eight hours. The extract was added to the aqueous acetone filtrate previously obtained. The acetone was distilled off and the phosphorus determined by Bang's⁸ modification of the Neumann method.⁹ The residue in the tube was dried, ground to a fine powder, and extracted with absolute alcohol and anhydrous ether for four hours each. The extracts were combined, the solvents distilled off, and the phosphorus in the residue determined. The amount was negligible. The residue was dried, powdered, and returned to the flask in which the precipitation had previously been performed, and there treated with 500 c.c. of a solution containing 1 per cent. of concentrated hydrochloric acid and saturated

⁸ Biochem. Zeitschr., 1911, xxxii, p. 443.

⁹ Zeitschr. physiol. Chem., 1903, xxxvii, p. 115.

with picric acid. The dilute hydrochloric acid dissolved all the inorganic phosphate, and the picric acid prevented the swelling of the protein. The mixture was shaken frequently, and, after at least sixteen hours, was filtered. After noting the volume of the filtrate, it was used for a determination of the phosphorus. The results were calculated to the original volume of 500 c.c. The residue, including the filter-paper, was also oxidized and the phosphorus determined. The amount was negligible, being approximately what was contained in the volume of liquid adhering to the protein and filter paper. That the method gives good results is demonstrated by the experiments previously reported.

As has already been explained, if the symptoms of paralysis agitans are due to parathyroid insufficiency, we may expect to find that the amount of acid-soluble phosphorus in the blood serum of such patients is greater than in that of other individuals. As is evident from the table, this is not the case. These results, therefore, do not support the view that parathyroid insufficiency plays a role in the etiology of paralysis agitans.

CONTENT OF PHOSPHORUS IN HUMAN SERUM. MILLIGRAMS OF PHOSPHORUS PER KILO OF SERUM.

Name.	Diagnosis.	Acetone extract.	Acid extract.
J. M.	Paralysis agitans	123.0	39.7
C. W.	Paralysis agitans	106.8	29.6
F. S.	Paralysis agitans	57.8	32.1
N. S.	Paralysis agitans	90.5	43.9
H. F.	Paralysis agitans	83.2	35.0
D. R.	Paralysis agitans	83.6	49.2
W. W.	Paralysis agitans	96.2	37.3
M. H.	Normal	{ 135.3	37.4
		{ 134.7	34.2
L. S.	Hysteria	101.8	34.5
R	Paraplegia, hysteria, cystitis	99.6	24.3
H. G.	Endarteritis	109.9	43.2
F. K.	Cataract, glaucoma	128.0	45.4
M. W.	Multiple sclerosis	81.6	36.9
J. H.	Multiple sclerosis	{ 117.3	47.2
		{ 113.8	47.3
E. D.	Multiple sclerosis	74.9	34.9
J. C.	Tabes	83.7	38.3
M. N.	Tabes	{ 99.1	40.5
		{ 99.7	42.4
H. S.	Hemiplegia	125.0	38.2

ON SOME ANGIONEURAL ARTHROSES (PERIARTHROSES, PARARTHROSES) COMMONLY MISTAKEN FOR GOUT OR RHEUMATISM.¹

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AMONG the diverse and often puzzling phenomena that, under appropriate exciting and determining influences, occur and recur in the subjects of angioneural imbalance (*vasomotor* or *autonomic ataxia*²), are pains and swellings in and around the joints. These are sometimes accompanied with fever; and, whether febrile or afebrile, the morbid complexus is commonly mistaken for gout or rheumatism.

Diagnosis and, in consequence, prognosis and treatment depend upon recognition of the underlying constitutional condition or diathesis. In other words, there must be a diagnosis of the patient, as well as of the particular collocation of symptoms that he (or she) happens to present at the moment. I have, before this Association³ and elsewhere,⁴ fully and repeatedly described the physical and functional characteristics and simple test reactions by which this diagnosis is to be made; and more recently Morichau-Beuchant⁵ in France, Herz,⁶ Eppinger and Hess,⁷ and Karl von Noorden⁸ in Germany, Barker and Sladen⁹ in this country, and

¹ Read before the Association of American Physicians, May, 1913.

² ". . . *Ataxia* rather than *hyperkinesis* or *hypokinesis*, because excessive vascular dilatation and excessive vascular constriction may be either spastic or parietic, or both spastic and parietic, as dilator or constrictor nerves, or both, are affected; and even in the extreme and opposite types of vasomotor ataxia, the phenomena, while always more or less paroxysmal, are neither exclusively those of dilatation nor exclusively those of constriction, but both abnormal dilatation and abnormal constriction are usually present in varying degrees in the same patient. The influences under which these phenomena are displayed are, more especially, temperature—and cold more than heat—emotion, visceral or external reflex excitation, and the action of toxic agents formed in the organism or introduced from without." From the author's paper of 1893. Cf. recent discussions anent "sympathicotonia" and "vagotonia." Following Langley's use of words, according to scientific precedent, I prefer to consider the autonomic or sympathetic system as a whole. Its fibers and ganglia may properly be classified according to function, upon pharmacological or other data—but to upset recognized terminology merely causes confusion.

³ S. Solis Cohen, *Vasomotor Ataxia*, Trans. Assoc. Amer. Phys., 1902, vol. xvii, p. 654 et seq.; *Visceral Angioneuroses*, Trans. Assoc. Amer. Phys., 1909, vol. xxiv, p. 527 et seq.; New York Med. Jour., February 19, February 22, March 5, 1910.

⁴ S. Solis Cohen, (a) *Vasomotor Ataxia*, Graves' Disease, Raynaud's Disease, Philadelphia Polyclinic, June, 1892; (b) *Vasomotor Ataxia*, A Contribution to the Subject of Idiosyncrasy, AMER. JOUR. MED. SCI., February, 1894; (c) Notes on Vasomotor (Autonomic) Ataxia, Med. Rev. of Rev., January, 1912; Graves' Syndrome, Raynaud's Syndrome, and Allied Disorders, Internat. Clinics, 1909, vol. iii, series xix, p. 41.

⁵ La diathèse angioneurotique, Arch. méd. Chi. du Poitou, December, 1908; Contribution à l'étude des idiosyncrasies, Le Progrès Méd., 1910, No. 16, p. 219.

⁶ Zur Lehre von den Neurosen des peripheren Kreislaufsapparates (Ueber Vasomotorische Ataxia), Berlin und Wien, 1902.

⁷ Zur Pathologie des visceralen Nervensystems, Zeitsch. f. klin. Med., 1909, lxvii, pp. 345 et seq., lxviii, pp. 205 et seq.; pp. 231 et seq.

⁸ Zur Kenntniss der vagotonischen und sympathikotonischen Fälle von Morbus Basedowii, Inaugural-Dissertation, Kiel, 1911.

⁹ Disturbances of the Autonomic Nervous System, Trans. Assoc. Amer. Phys., 1912, vol. xxviii, pp. 471 et seq.

others have in various connections repeated and somewhat amplified the descriptions. Among the writers cited, Herz and Barker and Sladen make due acknowledgement of the earlier observations.¹⁰

¹⁰ It may prove interesting, or at least amusing, to compare certain of the statements concerning vasomotor ataxia and its relations to idiosyncrasies, contained in the communication read by me before the First Pan-American Medical Congress (1893) and published in its Transactions (also in the AMER. JOUR. MED. SCI., February, 1894) with certain paragraphs in the paper published by Morichau-Beauchant in *Le Progrès Médical*, April 16, 1910, and in Herz's monograph of 1902. The sources of the citations are sufficiently indicated by their language—English, French, and German respectively. I have permitted myself to emphasize by small capitals in two of the French citations, and by italics in the German citation, an essential difference between the writers. The citations follow:

"For every idiosyncrasy there must be a physiological basis. By comparing the phenomena, special and general, exhibited by a group of persons presenting similar or identical idiosyncrasies, we take a step toward the recognition of the basic physiological conditions."

"I would invite attention to an idiosyncrasy of the circulatory mechanism, which, in its extreme degrees, manifests itself in the form of well-recognized symptom-complexes; in its minor degrees gives rise to puzzling manifestations of great variety of detail; and in its least developed forms often passes unnoticed. For this condition—which seems to depend upon a feebleness in the coördinating mechanisms, in consequence of which the balance of the cardiovascular action becomes disturbed by influences that in the great majority of persons have no such effect, and greatly disturbed by influences that normally have slight effect, while the restoration of equilibrium is slow and imperfect—I would propose the self-explanatory name of *vasomotor ataxia*. . . ."

"*Force nous est donc de faire intervenir une prédisposition spéciale, un terrain commun, qui permettra aux diverses manifestations qui ont fait l'objet de notre étude de se produire. Or, cet état morbide constitutionnel, nous avons donné le nom . . . de DIATHÈSE ANGIO-NEUROTIQUE.*"

". . . By the term *vasomotor ataxia* it is proposed to designate the condition of instability of the mechanism of circulation present in certain persons and characterized by abnormal readiness of disturbance, with tardiness of restoration, of the equilibrium of the cardio-vascular apparatus. The manifestations are most strikingly displayed by the heart and by the cutaneous peripheral vessels, but analogy indicates the occurrence of similar phenomena in the vessels of the glands and of the viscera, more especially in those of the kidney, of the gastro-intestinal tract, and of the brain."

"Vasomotor ataxia may be acquired as a sequela of disease; in many cases it is congenital; in some cases inherited; the condition is not rarely present in several members of a family."

"Among other symptoms and morbid associations observed are anemia, hysteria, drug and food idiosyncrasies, urticaria, local (circumscribed) edema, hyperidrosis, angina pectoris and pseudo-angina, organic heart disease, pulmonary tuberculosis, asthma, hay fever, vertigo, migraine, and other forms of headache, transient hemiopia and other visual disturbances, persistent mydriasis, . . . menstrual irregularities, intermittent polyuria, rheumatism, rheumatoid arthritis, contractures of digits, chorea, epilepsy, neurasthenia, neurotic dyspepsia, gastralgia, enteralgia, membranous enteritis . . . as effects of a common cause, or as secondary results."

"*La diathèse angio-neurotique, NISONS-NOUS, est une prédisposition morbide héréditaire et familiale caractérisée par une instabilité particulière de l'appareil vaso-moteur, qui rend celui-ci, chez les sujets qui en sont atteints, apte à répondre par des réactions excessives à des irritations qui chez d'autres resteraient sans effets. Son domaine est des plus étendus. Il comprend: des troubles du côté de la peau: urticaire, adèmes aigus circonscrits, érythèmes divers, auxquels s'ajoutent des manifestations nombreuses du côté des muqueuses et des viscères; crises gastro-intestinales, idiosyncrasies alimentaires et médicamenteuses, hypersensibilité de la pituitaire aux odeurs, asthme des foins et asthme vrai, migraines, etc.*

"Nur Solis-Cohen hat die Wichtigkeit, die Häufigkeit und die klinische Stellung der im weiteren zu schildernden Krankheitsbilder erkannt. Er nannte den sehr mannigfaltigen Zustand, welcher auf einer Schwäche in dem Coordinations-mechanismus beruht, infolge wovon das Gleichgewicht der Gefassaction von Einflüssen gestört wird, die bei der grossen Mehrheit aller Menschen keine solche Wirkung haben, und sehr gestört von Einflüssen, die normaler Weise nur eine kleine Wirkung haben, während die Herstellung des Gleichgewichtes langsam und unvollständig ist"—er nannte diesen Zustand *vasomotor ataxia*. Ich glaube dass dieser Name als kurze Bezeichnung beizubehalten ist."

"In many striking cases there has appeared to be morbid alteration in the thyroid gland." 卨

Il existe des présomptions en faveur de l'origine thyroïdienne des divers troubles relevant de la diathèse angio-neurotique.

The present communication may therefore be confined to a discussion of the special syndrome group to which it is desired once more to direct the attention of physicians.

In the title of the paper, the clinical pictures to be described have been designated *angioneural arthroses*. This term, however, is not entirely satisfactory. It implies, correctly, that the nosological species embraces several varieties. It indicates, moreover, that we are not dealing with true inflammation—*arthritis*. But it is not sufficiently comprehensive. In some, and perhaps the majority of cases, the edema of overlying tissues is more important than the effusion (or other change) within the joint; in still other cases the joint structures proper are not manifestly involved. For these the term *periarthroses*—or even *pararthroses* when it is only the neighboring soft parts that are affected—would be more suitable.

The term "*hydrops articularum periodica*" or "*hydrops articularum intermittens*" has been applied to the one variety of vasomotor joint disorder that has thus far been definitely recognized;¹¹ but it is applicable to that variety only. The number of varieties seems, however—as in all the related syndromes constituting the several species of the nosological genus *ataxia autonómica*¹²—to be limited only by the possibilities of variation; while the limits of variability approach closely the full extent of the possible permutations represented by the number of symptomatic and other factors.

To adopt the ancient Cnidian precedent and describe each variation of a variety as a separate species would, indeed, accord with the method of many writers upon neurovascular disorders; but my own endeavor for the last twenty-five years has been to group rather than to separate; to bring out the underlying unity rather than to accentuate the superficial diversity. Besides which, as I have repeatedly pointed out in regard to the whole subject, as well as to other special phases of it, such a course would ordinarily result in the ascription of a new diagnostic name to each recurrence of the disorder in nearly every individual. It is true that in a very few persons the successive attacks are relatively consistent—or rather, monotonous—in type; but this only emphasizes the general capriciousness and whimsicality of the phenomena.

The chief *symptomatic elements*, are pain, swelling, discoloration, and fever.

Pain and *swelling* are usually associated. They frequently develop, subside, and reappear together. Either, however, may be present without the other. Sometimes they alternate; sometimes they

¹¹ This was apparently first observed by Perrin (1845); then by Moore (1852, 1865). Fridenberg (1888) was the first American reporter. Schlesinger (1900) has made the most comprehensive study of the subject.

¹² Strictly speaking, autonomic ataxia is not a nosological genus in itself, but the substratum upon which a nosological genus is to be erected. As I have elsewhere shown, the several species arise out of the incidence, in the subjects of this condition, of diverse excitants and local determinants.

appear and disappear without any evident mutual relation. The extent of the swelling, moreover, is never an index to the degree or pain, whether directly or inversely; there may be intense pain with no swelling or considerable swelling with no pain. Either symptom may precede, either may outlast, the other.

The swelling may be *due* to effusion into the joint or to edema of the overlying soft parts, or both. Sometimes the painful joint and the tissues about it are not swollen, but a lump or lumps will appear on the limb, at a greater or less distance above the joint (*cardioid*).

The pain is ordinarily *referred* to the joint or joints apparently affected. Sometimes, however, it extends quite a distance along the limb, or is reflected to a distant point—most frequently, but not invariably, an articulation. Thus when the wrist is involved, the chief complaint may be of pain in the elbow, the upper arm or the shoulder—as a rule, of the same side, but sometimes of the other side—or even of substernal pain; or elbow pain may be associated with disturbed sensation in or around the mammary gland. The pain is variously described as burning, boring, stabbing, aching, or general soreness. It may be constant, remittent, or intermittent. Sometimes it is absent when the affected part is at rest and is experienced only upon active motion. In other cases it is aggravated even upon passive motion. In a few instances, the most gentle touch induces exquisite agony. This is especially marked at times when the costochondral junction is affected.

Numbness and tingling (“pins and needles” sensation) are frequently experienced in the fingers and toes; not only when these are themselves swollen and discolored, but also when their appearance is normal and the chief incidence of the disorder is elsewhere. *Paresthesiæ* of various kinds in any part of the body—thus in one patient always in the face and lips—most frequently, however, in the extremities—may be premonitory symptoms.

The skin of the affected part or of the limb at some distance from the joint to which the pain is referred, may be *discolored*. It is usually reddened; sometimes cyanotic, mottled, or pale and glistening; occasionally the seat of a papular, vesicular, or bullous eruption. Sometimes, however, there is no change of tint beyond that attributable to the distention. At other times there may be very slight and circumscribed swelling, but extensive reddish or purplish discoloration. The discoloration may be persistent. Ordinarily, however, it can be markedly lessened by gentle stroking in the direction of the venous current, or by elevation of the limb. When a terminal phalangeal joint is affected there may be ulceration at a nail margin. There may also be general or localized *erythema* of face, trunk or extremities.

Subjective *heat* in the affected part is common; but objective heat of a corresponding degree, or even sufficient to be detected by the touch of a normal hand, is relatively infrequent.

Fever is not common. When present it may be continuous, recurrent, or intermittent. It may show only as a rise of temperature, or there may also be headache, malaise, lassitude, and other constitutional disturbances. Headache or malaise or both may exist without elevation of temperature. In some persons there is both rise of temperature and constitutional disturbance, in every attack. In some there is rise of temperature only; in others, headache only. In some the pyrexia is preceded or followed or punctuated by chills or chilly sensations; or there may be chilly sensations without temperature change. In others there is never any febrile movement whatever; while still others may have fever in one attack and none in the next.

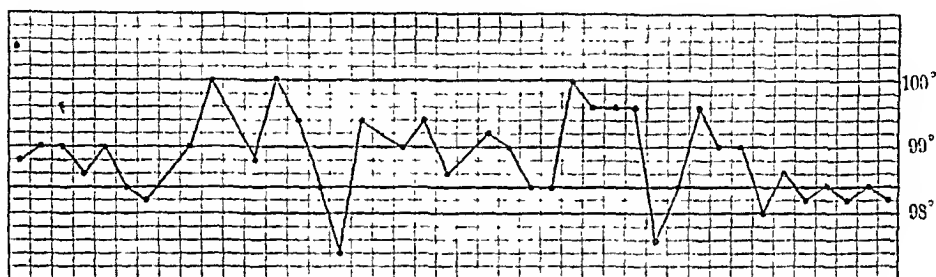


CHART I.—“Capricious” temperature curve in a case of febrile polyarthrosis of between two and three weeks’ duration.

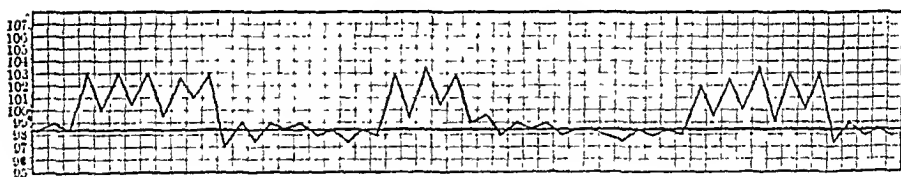


CHART II.—Portion of temperature chart from case of polyarthrosis showing irregular periodicity. The portion of chart reproduced shows two febrile periods of five days and one of three days, with one afebrile interval of five days, one of seven days, and portion of a third which was also of seven days.

In febrile cases the *temperature curve* is either entirely capricious—rising and falling without rhythm or apparent reason (Chart I)—or shows a curious tendency to what may be termed an irregular periodicity. Perhaps this might better be described as paroxysmal. As a rule the temperature rises suddenly and falls suddenly, when uninfluenced by treatment. (The times I saw it fall gradually I thought that treatment might be responsible.) The height varies. Ordinarily it is moderate, between 101.5° and 103° F. I have seen it reach 104.4° F.; and I have also seen it keep below 100° F. The time of maintained height may be a few hours or a few days, rarely a week. In most cases the temperature falls to the normal line, or to a point slightly above or below the normal line, in from twelve to seventy-two hours. Recovery may then ensue shortly, or after

a week or two, without further temperature rise. If the case be prolonged, however, the curve tends to remain low, with slight fluctuations, for a variable time—from a day or two to a week or more—and then again rises abruptly, and remains high, or with a sharp up and down movement, for two or three days or more, to subside as suddenly as it rose. This may be repeated several times in the course of a long attack; but in only one case did I observe an approximation to regularity in the periods either of intermission or of relapse. In that instance the free periods were five or seven days, and the febrile periods three or five days. There were four of the latter, the entire attack lasting about six weeks (Chart II). One would be inclined to separate the prolonged febrile cases from the afebrile and brief cases, did not the same patient exhibit at different times, both forms—and still other varieties.

Apart from the symptoms, the chief factors of the morbid complexus are *duration*, *recurrence*, *extent*, and *distribution* (or time and space).

The *duration* of a particular attack may be brief or prolonged—from a few hours to many weeks. It may be continuous, remittent, or intermittent.

Recurrence may be periodic or irregular, at short or long intervals—from days or weeks to months or years. Thus the patient may have four or five attacks every year, for two or three or more years; and then perhaps be entirely free for five or even ten or more years. Or daily or weekly brief attacks may continue for months, and freedom suddenly ensue, to be maintained for a few months or for several years. In this respect the condition parallels the more familiar angioneuroses of the skin and mucous membranes—urticaria, asthma,¹³ lingual and laryngotracheal (angioneurotic) edema, etc.

Extent may be slight or great; *distribution* constant or variable. In most of the cases of "hydrops articulorum intermittens" upon record, a single joint, and always the same joint, was affected in the recurrent attacks—in the majority of instances, a knee. In the slighter forms to which I desire to direct particular attention, and especially in those which involve rather the soft tissues about the joints than the articular structures, several joints may be affected simultaneously or in succession. A single finger-joint or a single toe-joint may indeed suffer, but this is comparatively uncommon. Recurrences may affect the same joint or group of joints, or different groups. No joint in the body is immune. I have seen three cases affecting the spine or overlying soft parts, at least two cases affecting the temporomaxillary articulation, and one case of cricoarytenoid involvement.

¹³ In hay fever and associated asthma the regular annual or other periodicity depends upon the regular annual (or other periodic) recurrence of the exciting noxa or noxae. That is a different matter.

The disorder is probably much more frequent than anyone has hitherto suspected. When I made my first special report upon the subject of articular and periarticular angioneuroses, to the College of Physicians of Philadelphia¹⁴ about two and a half years ago, I selected only six cases from records extending over twenty years, as instances which I then felt prepared to defend against sceptical criticism. Since I have studied the subject more closely I am convinced that I might have reported from those same records many times that number; but when one misses the opportunity to see the recurrences and is compelled to depend upon the imperfect sort of history obtainable from the average unobservant person, perhaps a judicious conservatism is not out of place. I am able, however, to add 21 new cases, making in all 27, distributed as follows as regards sex, age, fever, recurrences, and parts affected.

Sex. Males, 12 (44.5 per cent.); females, 15 (55.5 per cent.).

Age. Less than twelve years, 8 (29.6 per cent.); between twelve and twenty-five years, 12 (44.5 per cent.); between twenty-five and fifty years, 5 (18.5 per cent.); between fifty and seventy years, 2 (7.4 per cent.).

Attacks. Observed in one attack (or series¹⁵) only, 13 (49.5 per cent.). Observed in several attacks (or series) 14 (50.5 per cent.). Total number of attacks (or series) observed in or reported by 27 persons, 110.

Fever. Febrile in all attacks, 5 (18.5 per cent.). Febrile in one or more attacks, but not in all, 6 (22.2 per cent.). Afebrile throughout, 16 (59.3 per cent.).

Parts Affected. Joints only, 3 (11.1 per cent.). Soft tissues only, 8 (29.6 per cent.). Joints and soft tissues, 16 (59.3 per cent.).

Distribution. Multiple in several attacks, 16 (59.3 per cent.). Multiple in one attack only, 3 (11.1 per cent.). Mono-articular in all attacks, 8 (29.6 per cent.).

*Intra-articular Affections.*¹⁶ Spine: cervico-occipital, 1. Face: temporomaxillary, 2. Extremities: wrist, 6; knee 3.

Intra- and Peri-articular Affections. Crico-arytenoid,¹⁷ 1; temporomaxillary, 1; lumbosacral, 1; sternoclavicular, 3; chondrosternal, 2; vertebrocostal, 4; shoulder, 5; elbow, 10; wrist, 14. Hand and fingers: metacarpophalangeal, 14; interphalangeal, 16;

¹⁴ S. Solis Cohen, Angioneurotic Manifestations in and Around Joints, Frequently Mistaken for Gout and Rheumatism. Trans. Coll. Phys., Philadelphia, 1911, series iii, vol. xxxiii, p. 309 et seq.

¹⁵ Case I illustrates what is meant by a *series*; it is, of course, several brief attacks with short intervals, but to record it as twenty or more attacks seems inappropriate.

¹⁶ The figures in intra-articular affections, intra- and peri-articular affections, and peri-articular affections are not comparable with any others in the present records, since they include both multiple and mono-articular attacks and recurrences in cases in which different joints and groups of joints were involved each time, or in which at one time joints only, at another time *soft tissues* also, were affected.

¹⁷ Laryngoscopic appearance.

hip, 1; knee, 9; ankle, 8; heel, 4; toes: metatarsophalangeal, 6; interphalangeal, 3.

Peri-articular Affections. Acromioclavicular, 1; shoulder, posteriorly, 1; hand and fingers, 10; foot and toes, 6; wrist, 7; lumbosacral junction, 2; costochondral junction,¹⁸ 4.

The foregoing figures are given more to accord with conventional methods of reporting, than because I attach any great significance to them. The total number of individuals is too small, and too many accidental factors enter into the statistics, to permit this.

Thus as regards age, for example, it so happens that I saw certain persons in childhood, others in adolescence, middle life, advanced age. Yet I feel sure that in a much larger proportion than indicated, the disorder manifests itself before the twentieth year, perhaps before the twelfth year. Ordinarily, however, it is not recognized. The present report gives, therefore, only the ages at which the patients were first seen by a certain observer. Again, however confident I may be that the history frequently given, of previous attacks of "rheumatism" or "gout" (not seen by me) really refers to the condition under discussion, I have felt justified in so recording those attacks in only about one-third of the instances. An error of judgment here, whether of omission or of commission, necessarily affects the statistics of fever, of recurrence, and of distribution. There is also a possibility of error in the anatomical diagnosis in the exclusion or inclusion of intra-articular effusion in the mixed cases.

CASE REPORTS.

Case reports sometimes convey a more vivid picture than a general description with its necessary qualifications; but in a disorder so multifarious in aspect as that under consideration, reports *in extenso* are out of the question.

From the 27 cases, however, some 7 may be selected for brief narration, as illustrative at once of the great variety in detail of the morbid pictures and their essential sameness in fundamentals.

CASE I.—*Intermittent, afebrile swelling of hands and wrist, with pain in upper arm; daily paroxysms in each series; monthly recurrence of series.* Ethel X., schoolgirl, aged thirteen years, complains of paroxysmal attacks of pain and swelling in the hands, with pain in the upper part of the arm. The trouble began two years ago. It usually affects one side only—and more frequently the right—but occasionally is bilateral. The swelling occupies the palmar surface, affecting chiefly the metacarpal-phalangeal articulations and overlying parts, including the hypothenar eminence. The

¹⁸ Probably periosteal edema. I have also seen several cases of periosteal edema at a distance from joints, which are not included in the present paper.

dorsum is not involved. Occasionally the process extends to the wrist, which it encircles. Whether from pain or mechanical obstruction by the swelling, or both, it is impossible to close the hand. The affected parts are discolored (mottled red and purple) and swollen. They are subjectively, but not objectively hot, and are not especially tender to pressure unless it produces passive motion. There is no fever. Sometimes there is pain in the thigh, and also (but rarely) in the foot as well. Swelling or discoloration, however, has not been observed in the lower extremity. The attack lasts from one to twelve hours. If prolonged beyond an hour or two, there will be remissions or intermissions. The paroxysm may occur daily, though not always at the same hour, for three or four days in succession. Until recently there would be a period of freedom of a month or more; but now the free interval is seldom longer than a week.

The child has not yet menstruated. She shows quick, hyperemic dermography, has typical tricolored nails, and exhibits slight retraction of the upper lids upon fixation of the eyes in convergence (Cohen's eye-sign). There is no tremulousness of the lids, and no lagging. The girl becomes car-sick easily and vomits, but never has sick headache. At times she has bilateral, temporal headache. She perspires readily, even in cold weather. During a paroxysm of pain and swelling the palmar surfaces perspire freely. They are purple or mottled at that time, while the dorsum of the hand, and the wrist, even if swollen, are red. The girl thinks the attacks are more frequent in cold weather; nevertheless she prefers winter to summer, as she becomes faint and is drenched with sweat on slight exertion in warm weather. There is no discoloration except during the attacks of pain and swelling. There is no lesion of the heart and no palpitation. The thyroid is not enlarged. The blood pressure is 110 systolic and 75 diastolic. The bowels are usually constipated. The urine shows an occasional trace of albumin following an attack.

The mother of this patient is aged forty-four years. Three months ago she was subjected to a vaginal hysterectomy for myoma. She now complains of puffing of the fingers at night, with pain, which subsides during the day. This was preceded by similar pain and swelling in the left breast, which, however, came during the day and disappeared at night. She was seen but once, and at that time the hands were red and slightly swollen, the color running out and the swelling tending to disappear, upon elevation. The urine shows neither albumin nor sugar. She is a typical subject of *autonomic ataxia*.

The elder sister of the patient (also a typical *autonomic ataxia* subject), aged nineteen years, began to sneeze and present a hay-fever picture shortly after the family removed from Philadelphia to the interior of New Jersey. This, however, was in October,

and the attack subsided in a short time. It recurred in June and lasted until she went to New York City in July, when it ceased after two or three days, but returned when she came home in September. It was ascertained that this girl was susceptible to "ivy" poisoning, and that there was considerable "poison ivy"¹⁹ near the house. When this was cut down, the sneezing and associated symptoms ceased. Curiously, the younger girl who exhibited the angioneural arthrosis and dermatosis was immune toward "ivy."

Two maternal uncles have asthma, and one of these has had attacks of giant urticaria. On the father's side there is nothing significant.

CASE II.—*Afebrile, paroxysmal, intermittent joint pain, in fingers chiefly, of brief duration, at first recurring fortnightly or monthly; later assuming nightly periodicity, with redness and swelling; later becoming premenstrual and associated with chilly sensations and blueness of the extremities.*

Mrs. X., aged twenty-eight years, housewife, has been married six years and is the mother of two healthy children, the youngest of whom is two and a half years of age and has been weaned for a year. The chief complaint is of pain in the joints, principally those of the fingers, which at the time of examination are tender and swollen and have been so, off and on, for two days. The left hand only is affected at this time. All the metacarpophalangeal joints and the first interphalangeal joints of the first, second, and third fingers are involved, together with the overlying tissues. The soft parts of the dorsum of the hand and wrist are also red, tender, and swollen. The patient states that the pain first appeared some time during her first pregnancy, coming on without warning, and lasting, with intermissions of an hour or two, for a couple of days, after which she was free for a fortnight, when it recurred in the same way. Unfortunately I have no exact note of the conditions preceding and following delivery and the establishment of lactation. Apparently these events had little influence; nor was any change brought about by the return of menstruation. The pain continued to recur paroxysmally, fortnightly or monthly, without apparent definite relation to the reestablished menses. This pain is described as a dull ache, with occasional sharp exacerbations. At first it did not keep her awake. The hands and fingers were tender to the touch, but at this time were not red nor swollen nor hot. The trouble continued, despite treatment, until some time during the second lactation, when it became much worse, and assumed new features. The pain would come on shortly after 6 P.M. daily and last until she fell asleep, frequently

¹⁹ Identification of the noxa is not certain. The father was told to bring me a leaf, but did not do so.

waking her during the night. At this time, also, swellings began to appear, at first occasionally, then with each recurrence of pain. The pain and swelling affected principally the knuckles and phalanges, but also at times the wrists, the knees, and the ankles. The toes were never involved. The two sides of the body were rarely affected at one time, but the hand and knee, or the knee and ankle of either side might be painful or swollen in coincidence or in quick sequence. Sometimes a hard lump would develop on the hand or arm, at some distance from the joint, or a bruise-like patch would appear; or there might be both swelling and discoloration. The swelling did not pit upon light pressure. The spot was never red, nor did it have a red areola, nor was there any itching, but it was always tender to pressure. At no time was there fever, but there had been gradual loss of appetite and wasting. Treatment with baths and massage seemed to aggravate rather than relieve. Suddenly a period of freedom ensued, which lasted for several months. During the summer preceding her visit to me, the patient had felt entirely well, and had regained flesh to within a few pounds of her former weight. About three months before she consulted me the trouble had returned, but again with a different aspect. This new series of phenomena would come on three or four days before the menstrual period, and would be relieved with the appearance of the flow. It would begin with general chilliness, the feet would become "cold as ice," the hands and ears blue, but not cold. The tip of the nose would become blue or white. After a few hours, the finger-joints would become stiff and painful, then red and swollen, and, at times, hot. With this, the cyanosis would disappear; but the feet remained cold. There had been but three such attacks. In the first, both hands had been involved at once for four days; in the second, the right hand for two days and the left for two days; the third attack was the one I saw. The left hand only was involved for two days. The next day the patient complained of pain in the throat, with difficulty of phonation. Laryngoscopic examination showed swelling and redness of the right vocal band and arytenoid eminence, which subsided in great part under a spray of epinephrin solution.

This patient presents the typical dermatographic, ocular, and nail-bed signs of *autonomic ataxia*. She is not hysterical, but is easily startled. Among the other life-long phenomena of vascular imbalance is a tendency to perspire, even in cold weather, and paroxysmal, apparently causeless, flushing of the face and ears, with "pins and needles" sensation in the lips and ears or sometimes in the extremities. The hands frequently become blue or mottled on going out of doors in cold weather. There is slight enlargement of the thyroid gland. There is pain on pressure, both in the supra-orbital and infra-orbital notches. There is no heart, lung, or kidney lesion. Information concerning other members of the family is lacking, except that

the mother suffered with menstrual migraine and one sister died of pulmonary tuberculosis.

CASE III.—*Recurrent mono-articular swelling of the knee; afebrile.* A. C., male, insurance agent, aged forty-one years; has had recurrent swelling of the right knee, without spontaneous pain or fever, for two years. It comes and goes suddenly without apparent reason. The swelling is evidently intra-articular, the patella floats. There is no redness, no tenderness, no heat. The attacks last from a day or two to a week, disappearing more quickly if the patient rests. There is pain upon motion only. The intervals of freedom vary from four to six weeks. The patient exhibits the signs of *autonomic ataxia*. He is of a gouty family and has had uriticaria repeatedly. He has never had rheumatic fever or polyarthritis of any kind. There is no history of gonorrhea or syphilis. The patient recalls no injury to the part. There is no cardiac or renal disease. There is considerable susceptibility to drugs, especially salicylates, quinine, and iodides.

CASE IV.—*Recurrent, intermittent polyarthrosis, with coincident edema of soft parts; febrile manifestations.* Mrs. L., aged thirty-eight years, housewife, has been under my care for twenty years, and during that time has exhibited many and various syndromes of vasomotor disturbance (including many so-called "drug and food idiosyncrasies"—anaphylaxis?). Also, her mother, brother, sisters, and children exhibit the same sort of susceptibilities. During my absence from the city in 1905 she was treated for what was called "articular rheumatism" by a physician unacquainted with her constitutional characteristics and tendencies. Since that time she has frequently had attacks of pain and swelling, sometimes affecting one joint, sometimes a group of joints, and occasionally exhibiting tenderness and redness, but never heat, of the overlying soft parts. These phenomena have usually been transient, lasting an hour or two, or at most twelve hours, but sometimes continuing for two or three days with or without intermissions. No periodicity can be traced in the recurrences, these being, as a rule, coincident with emotional disturbances—"servant troubles," sickness of husband or children—or with fatigue from zealous housecleaning or prolonged dancing or "bridge," etc. Occasionally the attack has followed some dietary indiscretion. In the fall of 1910, following the prolonged incidence of measles and whooping cough among her children, during which time she had little rest, the patient complained of great pain in the left wrist, which was swollen, red, and tender, but not hot. She was anemic and weak, and was ordered to bed, but did not go. The next day both wrists and the fingers of the left hand were involved, and there was fever (103° F.). This is the case giving the curious temperature curve shown in Chart II. The pain and swelling in the joints continued with periods of exacerbation and

remission for six weeks. The last period of high temperature (there were four in all) ended in the fifth week. No connection could be traced between increase of temperature and aggravation of local phenomena, for the joints might be painful and swollen when the temperature was low or when it was high—and conversely. During the course of the attack, both wrists, both elbows, the fingers of the left hand, the toes of both feet, the right ankle and the right knee were involved; the wrists almost continuously, the other joints intermittently. Tingling in a part often preceded the swelling by twenty-four hours. At first there was considerable spontaneous pain in the affected joints; but for the most part the pain lessened or disappeared the day after the swelling developed, and would remain absent except upon active or passive motion or pressure, when it became, at times, very severe. During and after convalescence, "pins and needles" sensations in one or another extremity or in the rectum, were frequently complained of.

CASE V.—*Recurrent, afebrile, monodigital, swelling and pain, associated with a bullous eruption, occurring in a gouty subject.* Mr. P. S., manufacturer, aged fifty-five years, belongs on the paternal side to a gouty family and has had several attacks, both in hands and feet, of what was diagnosed as gout by his former attendants. I have not seen him in a true gouty attack in the five years that he has been under my care. His finger-joints are more or less thickened, but they have not become swollen or tender, except in the following manner: One finger—usually, but not invariably, the left index finger—begins to tingle and changes color. Ordinarily it becomes paler than normal, but sometimes it takes on a purplish hue. Pain now develops. The first joint swells, the skin reddens, and the swelling gradually spreads until nearly the whole finger is involved. The pain subsides. A number of small transparent vesicles appear, which apparently coalesce into fair-sized bullæ. These dry up, as a rule, without rupture unless the finger receives an inadvertent knock, in which case they may break, exuding colorless, odorless, unirritating fluid. The swelling subsides, the color disappears, and in the course of a week the finger has resumed its former condition. These attacks recur irregularly, there having been six in five years, but with one free interval of nearly three years. There is no organic disease; no recent gonorrhœal infection; no evidence of persistent infection; no history of lues. The attacks have sometimes seemed to be provoked by indiscretions in diet. The patient, one son, and one daughter present the signs of vascular imbalance. The daughter recovered some ten years ago, under my care, from pulmonary tuberculosis, which exists in the patient's family on the maternal side.

CASE VI.—*Intermittent and sometimes painful swelling of soft parts about gouty finger-joints, about acromioclavicular articulation, intermittent mammary swelling, and along trapezius border and*

spine of scapula; occasional fever; Mrs. R., aged seventy years, has a life-long history of gouty and nervous symptoms of various kinds. Her finger-joints are enlarged, often painful, and some of the fingers stiffened. She is subject to sudden burning and itching in the throat, accompanied with intense redness of the mucous membrane of the palate or pharynx, and subsiding in from ten to thirty minutes, or at most an hour. The sublingual veins swell suddenly and as suddenly return to their usual state. There are numerous little venous nodules along the right border and inferior surface of the tongue. The left pupil is ordinarily dilated, but at times suddenly returns to the normal size, or may be contracted. There is excessive retraction of the upper eyelids not only upon convergence, but also spontaneously during the excitement of interesting conversation. Dermographism is readily produced upon the patient's smooth, white skin. At times during the past ten years or more, the soft parts over one or more of the gouty finger-joints swell. As a rule, the swelling is painless—but occasionally there is pain and redness. This may last for a day, or intermittently for a week. It may recur frequently, or after an interval of many months. More recently there are sudden seizures of intense pain in the upper left arm, followed by swelling along different portions of the neck and shoulder, most frequently over the acromioclavicular junction, or along the outer border of the trapezius, or above the spine of the scapula. These may be painful and are always tender, but never reddened. They appear suddenly, and ordinarily subside in from twenty-four to seventy-two hours. Sometimes they may last, with remissions, the better part of a week. Six such attacks have occurred in two years, the first four within six months. Two of them were associated with slight fever. The first attack was attributed by the patient to "cold." She is careful in diet, and the bowels are regular. There is no evidence of neuritis. There are no symptoms of angina. While there are periods of indigestion, and also periods of increased and diminished uric acid and urate output, no connection can be established between these and the swellings referred to. The patient states that at times her breasts (which are well-preserved) swell, but without pain. I have never seen this condition of the mammæ as it seems to subside very quickly. There is exophthalmic goitre and epilepsy in the mother's family; cancer and apoplexy in the father's family. The patient's bloodvessels are unusually soft for her years, and she has no disease of the viscera.

CASE VII.—*Afebrile, recurrent joint pain associated with numbness under left breast and with nausea.* Mrs. G., aged twenty-five years, has been feeling badly for six years. She has attacks of palpitation; frequent sick headache; constipation; at times, paroxysmal dyspnea. She cannot eat strawberries, as this provokes hives. During the last year there have occurred "spells" of intense pain in the left

elbow, aggravated upon motion. The pain lessens after half an hour or so, but does not disappear entirely for several hours. There is no swelling, tenderness, heat, or redness. The pain is preceded by tingling and numbness in the left ear, and followed or accompanied by numbness and stabbing pains under the left breast. With this last comes a feeling of faintness and nausea, but without vomiting, nor does the provocation of vomiting relieve it. There is no fever. The spells may come daily for several days, and then disappear for weeks. They bear no ascertainable relation to menstruation or constipation or other symptom, directly or inversely. There is no evidence of any organic disease whatever, no history of gonorrhea or syphilis. The patient shows the dermatographic, ocular, and nail signs of *vasomotor ataxia*; the thyroid is not enlarged; there are numerous petechiæ and telangiectases on the body; pilomotor reflex is marked; she bruises easily and formerly bled from the nose. Glasses seem to have lessened the frequency of the headaches, which now occur only at the menstrual time, and not with every period. Four years ago the patient was operated on for appendicitis. The family history is not obtainable.

Diagnosis.—From what has been said, and from the histories given, both the difficulty and the ease of diagnosis should be evident. To mistake the condition for gout, rheumatism, muscular rheumatism, myalgia, neuralgia, neuritis, etc., is common, and is, indeed, excusable, so long as one's attention has not been directed to the subject; and the subject is ignored by most text-books and systematic writers. In members of gouty and rheumatic families and in hysterical subjects the discrimination may be peculiarly difficult—and just such persons yield the majority of the cases. I have elsewhere²⁰ discussed this relationship, as well as that of hysteria, neurasthenia, tuberculosis, cancer, diabetes and epilepsy, to autonomic disorders in general.

In *afebrile* cases the chief elements in diagnosis are the recurrent tendencies of the disorder, the family and personal history, and the characteristic signs of constitutional peculiarity²¹ (idiosyncrasy) exhibited by the patient.

In *febrile* cases, the discrimination from rheumatic fever is at first difficult. A knowledge of the patient and his family helps, but may also lead astray, since a subject of autonomic ataxia is as liable as any other person to rheumatic infection. In the absence of authoritative bacteriological, serological, or other exact tests for infective polyarthritis, the diagnosis becomes evident only as the case proceeds. It must be based on all the phenomena, not on any one point. Considerable reliance, however, may be placed on the temperature curve, which, as pointed out, may be utterly capricious or exhibit certain more or less well-defined phases, or even

²⁰ Cohen, loc. cit.

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²¹ Cohen, loc. cit.

an apparent periodicity. Marked increase of eosinophiles or a disproportionately low count of polymorphonuclear leukocytes, or a marked excess of urinary indican or ethereal sulphates, favors the diagnosis of angioneural disturbance, but is not conclusive. Nor are any of the reverse conditions conclusive negatively.

Some patients cannot bear salicylates, and, as a rule, these compounds, even when well borne, are less efficacious in relieving pain than in true rheumatism. They are not, however, entirely devoid of palliative effect, and hence a conclusive "therapeutic test" is not available.

The result of medication may be taken into consideration with other evidence—that is all.

Treatment must be individualized. It is more efficacious in prolonging the intervals of freedom, and perhaps finally overcoming the tendency to recurrence, than in controlling—except palliatively—the special attack or series of paroxysms. Indeed its influence over the special attack is hard to estimate.

During the *acute stage* the chief elements of treatment are rest (local and sometimes general), regulation of diet,²² elimination, and (relative) antisepsis. In some cases, special medication (and local applications) of a symptomatic and palliative character may be needed.

During *convalescence* from prolonged febrile cases the administration of roborants and hematinics is desirable.

During the *intervals of freedom*, treatment must be directed toward prevention. To this end, measures for reëducating the vascular reactions and for restoring the tone of the vasomotor centres must be instituted; and the special exciting and determining factors, intrinsic and extrinsic, of the individual case, must be sought out and avoided or combated. In addition to the carefully individualized regulation of life and diet, persistent elimination, antisepsis, applications of hot and cold water, sometimes massage and high frequency electric currents or discharges, and the administration of angiotoxic medicaments (including the preparations and products of the glands of internal secretion) are thus among the measures applicable.

To discuss these therapeutic expedients in detail is impossible within the limits of the present article. It may be said, however, that much can be accomplished by persistence in treatment along well-thought-out lines and with measures and methods carefully adapted to all the circumstances of the individual case. This is capable not only of giving a considerable degree of relief, but sometimes seems to overcome, in great measure, the morbid tendencies.

²² For the first day or two in the more severe cases, and especially in what seems likely to be a prolonged febrile attack, the diet should consist chiefly of skimmed milk or whey with hot water to which sodium chloride (0.1 per cent.) and sodium bicarbonate (0.2 to 0.4 per cent.), and perhaps a little lemon juice, may be added. Later, barley water, sour milk, pancreatized milk, "one-minute" eggs, junket, pancreatized gruels, etc., may be given; and still later, fresh fruit and green vegetables. Meat and fish should be avoided.

LEUKOPLAKIA OF THE PELVIS OF THE KIDNEY AND ITS DIAGNOSIS.

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METAPLASTIC changes in the mucosa of the urinary tract, ending in leukoplakia or epidermization, are said to be very uncommon. According to the literature of this subject there are only 44 reported cases of leukoplakia of this system. Of these, 9 cases occurred in the pelvis of the kidney (to this must be added the recently reported case of P. Lecene;¹ 27 cases occurred in the bladder and 8 in the urethra. In view of the fact that I have seen 5 cases of leukoplakia of the bladder and pelvis, I suspect that the above statistical statement is not a truthful expression of the frequency of this condition in the urinary tract. Though this type of change in the mucosa does not give rise to symptoms with any regularity, in one of the cases that I wish to report well-marked symptoms were produced by the peeling off of the surface of the metaplastic patch in the upper urinary tract. J. Englisch² reviewed the literature of this subject completely, and brought together the 9 cases in the upper urinary tract. They were reported by Leber (four months old case, bilateral), Chiari (thirty-four years old, with an indigo calculus), Halle (associated with a calculus), Braatz (thirty-three years old, associated with infection), Rona (thirty-five years old, associated with calculus and tuberculosis; also another case, in a patient aged forty-six years associated with tuberculosis), Beselin (eighteen to thirty years, associated with tuberculosis), etc. The recent case of Lecene was aged twenty-eight years, and was associated with infection. Thus it is evident that in almost every recorded case there was an associated condition, either a calculus or simple or tuberculous infection. In the two cases reported in this paper one was associated with tuberculosis, and the other, as far as determined up to date, is an uncomplicated case of leukoplakia. In view of the apparent rarity of the condition, and in view of the fact that only one other case of leukoplakia of the upper urinary tract, which gave rise to symptoms, is on record, I have decided to report these cases briefly:

CASE I.—M., aged twenty years. This patient had suffered from an orthostatic albuminuria, and at the age of seventeen years had an attack of cystitis that was quite rebellious. All the tests for tuberculosis were then made, with a negative result. Shortly

¹ Jour. de Urol., February, 1913.

² Zeitsch. f. Urologie, 1907.

thereafter he had some vague pains and tenderness in the left lumbar region, which suggested the possibility of a calculus, but the x-ray examination was negative. From that time on he was well for over two years, when a sudden attack of left renal colic set in. He was up and about in a few days. Nothing abnormal was noted in his urine, and another x-ray taken at this time was negative. A few days later I saw the patient on his return to town, and noted a distinct tenderness along his left ureter and over the left kidney. Following this examination, another attack of left renal colic set in. All the urine was saved from this time on. Macroscopically the urine was normal in color, but floating around in it were pearly white membranes, looking like paraffin shavings, about one-quarter of an inch square, rolled on themselves, and settling slowly to the bottom on standing. Closer examination of these membranes showed that the pearly white appearance was limited to one side only and that the other side was in part white and in part light brown in color. To this side some crystals were adherent, and these, plus other similar crystals found in the sediment responded to none of the tests for phosphates, oxalates, urates, uric acid, lime, magnesia, cystin, xanthin, and were, without much doubt, according to the examinations of Dr. S. Bookman, silicates. The membranes obtained after this and a subsequent colic were further examined under the microscope, and showed the picture of surface exfoliated epidermis (Dr. F. S. Mandlebaum). The original suspicion, on seeing the membranes floating in the urine, was thus confirmed by more extensive investigation. In addition to these membranes and crystals, the urine contained many epithelial cells, some pus, some red cells, a few granular casts, and a few cholesterin crystals. Cystoscopic examination showed two normally placed ureter openings, and close to the right ureter another very small opening from which the indigo-carmin stained stream was feebly projected. The left ureter opening was swollen and moderately bruised looking, as one sees so regularly after the passage of a calculus. Both kidneys discharged the indigo-carmin normally, and the bladder wall was otherwise normal, showing no signs of epidermization or leukoplakia. The specimens obtained from the kidneys showed many epithelial cells and few pus and red cells. Both specimens were sterile and they were injected into guinea-pigs, two being used for the left and one for the right. No tubercle bacilli were found and all pigs were negative. Following the catheterization of the kidneys, another attack of left renal colic set in, probably due to the fact that I had loosened some more membrane by pushing the catheter well into the pelvis of the left kidney and washing the same with several syringefuls of solution. During this colic the patient did not suffer as much as do those that pass a calculus, but following it we recovered from his urine the largest piece of membrane seen up to date. It

was laminated, and consisted of four layers of pearly white membrane rolled up one within the other, as seen in cholesteatomas in other parts. This piece was fully $\frac{3}{4}$ by $\frac{1}{3}$ inch in size, and caused some trouble in passing through the urethra. During the past three months the patient has had no further attack.

REMARKS. From the above facts it is evident that we are dealing with an exfoliative process, which from the nature of the specimens studied can only be an exfoliation from a surface of leukoplakia. It is of interest to note that silicates were found in the urine, and that these salts in the human body are found mainly in the skin appendages, *e. g.*, hair, nails.

The only similar case in the literature comes from Czerny's clinic published by Beselin (1885). This was a man, who from the age of eighteen to thirty suffered from right-sided pains, which came on in attacks, with sweats, vomiting and irritation of the bladder. His urine contained white fragments of tissue made up of flat epithelial cells and cholesterin crystals as well as pus and red cells. He had 200 such attacks, and after the attacks the urine contained pearly white, shining masses (Schollen), in which the deeper cells alone had nuclei, and in which the cell bodies were indistinct. The kidney was removed on the diagnosis of a dermoid which had broken into the upper urinary tract. The patient succumbed to a peritonitis. The specimen showed that the pelvis was filled with a pearly white membrane, in part loose and in part loosely attached to the underlying wall of the pelvis down to the ureter. The cholesteatomatous formation was as usual arranged in leaves. Otherwise the kidney was the picture of a tuberculous pyelonephritis, but no tubercle bacilli were recovered.

CASE II.—M., aged thirty-five years. Sick nine months, with pain in left flank, radiating to scrotum. The pain was dull in character. Two months before admission there developed increased frequency of urination, associated with pain and occasional hematuria. The diagnosis of a renal tuberculosis was made from the catheterized specimens and the kidney was removed. The kidney was twice as large as normal, and converted into a pyonephrosis. There was tuberculous destruction of the papillæ, as well as tubercular foci in the cortex. In the lower half of the pelvis there was an area of leukoplakia of irregular shape, about the size of a silver dollar. This was a little below the surface of the adjacent inflamed mucosa, and pearly white in appearance. No membranes were attached to this surface.³

* A colored illustration in the article by Lecene gives an excellent idea of the appearance of this lesion.

THE INHIBITORY ACTION OF CERTAIN ANILINE DYES UPON BACTERIAL DEVELOPMENT.¹

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FIRST COMMUNICATION.

A. HISTORICAL REVIEW. While Pfeffer² had demonstrated in 1886 that certain aniline dyes are capable of producing a harmful effect upon the higher plants, Rozsahegyi³ seems to have been the first to point out that a similar effect is exerted upon certain bacteria (1887). His experiments were conducted by embodying the dyes in nutrient gelatin and inoculating the tubes with the different organisms. The number of the dyes as well as of the types of bacteria which were studied is not large (carmine, methylene blue, gentian violet, vesuvin, fuchsin, and methyl violet in reference to the *Bacillus cyanogenus*, *pyocyaneus*, *cuniculicida*, *cholerae gallinarum*, *murisepticus*, *cholerae Asiaticæ*, Finkler-Prior and *cholerae suum*), but the writer has clearly demonstrated not only that certain organisms do not develop in the presence of certain dyes, but also that certain dyes possess a *selective* action for certain organisms. He has thus pointed out that while the bacillus of rabbit septicemia readily grows in the presence of carmine and vesuvin, and not in the presence of gentian violet, the chicken cholera bacillus does not grow in the presence of vesuvin, but does so without difficulty in the presence of gentian violet. He accordingly suggests that this method may be used to advantage in differentiating similar bacterial species from one another.

Rozsahegyi's experiments very curiously seem to have escaped the attention of a number of subsequent investigators, and Stilling in particular, whose detailed investigations into the bactericidal action of aniline dyes were published in 1890, does not mention them. It appears, however, from the meagre literature upon the subject that the inhibitory effect of certain dyes upon bacteria was known to a number of observers, even though the observation of this fact led to no further investigation. Cornil and Babes⁴

¹ Received for publication April 15, 1913.² Ueber Aufnahme von Anilinfarben in lebende Zellen. Untersuchungen aus d. botanischen Institut in Tübingen, 1886, ii.³ Centralbl. f. Bakt., Orig., 1887, ii, 418.⁴ Les bacteries, 1890, third edition, i, 76.

thus mention in the third edition of their work on bacteria that the movements of certain organisms are arrested when these are placed in aqueous solutions of certain dyes, but they evidently also noted the selective action of their staining solutions, for they remark that the cholera vibrio remains alive even after being stained.

Krcmianski,⁵ of Charkoff, further advocated the use of pure aniline and of aniline dyes, as inhalations in the treatment of phthisis, upon the basis of their bactericidal power. Incidentally it is interesting to note that a curative action of aniline upon wounds has long been assumed by aniline dye-workers, who are in the habit of dusting abrasions, etc., with dyes, and maintain that the healing process is thereby hastened.

In 1890 there appeared three publications dealing with the bactericidal action of aniline dyes, viz., one by Penzoldt,⁶ who records the investigations made under his direction by Beckh, and two others by Stilling.⁷ Beckh found that methyl violet, malachite green, and rose Bengale (in aqueous solutions, varying in strength between 2 and 10 per cent.) would kill staphylococci, and that trimethyl rosaniline, phenyl blue, and methylene blue (in 0.2 to 3 per cent. solutions) will inhibit their development, or may even arrest it completely, while (acid?) fuchsin, corallin, eosin, methyl orange, vesuvin, tropeolin, scarlet red, and indulin are without effect. The experiments were carried on by impregnating silk threads with the organisms and then planting them in nutrient gelatin containing the dyes in various concentrations. The same observer notes that concentrated solutions of methyl violet, malachite green, trimethyl rosaniline, and phenyl blue prevent the growth of the anthrax bacillus.

Stilling has been less explicit in reference to the names of the individual dyes which he investigated. In his first publication he remarks that "certain aniline dyes, notably those of violet color, possess all the properties which one can demand from a good antiseptic" (p. 6). In a foot-note (p. 8) he states, "For brevity's sake I shall use the term methyl violet to designate the entire group of violet aniline dyes." In addition to these, still others were tested, however, for he mentions at one place (p. 12) that fuchsin, methylene blue, rhodamin, vesuvin, and many others were examined, but that none of these were as efficacious as the violets. The next best were certain auramins. Etyl violet he found even more active than "methyl violet," but as this is contaminated with arsenic it could not be used in his animal experiments, nor in his therapeutic investigations. At Stilling's request

⁵ Cited by Stilling, second communication, p. 4.

⁶ Arch. f. exper. Pathol. u. Pharmak., 1890, xxvi, Heft 5 und 6.

⁷ Anilin Farbstoffe als Antiseptica und ihre Anwendung in der Praxis, Mittheilung 1 and 2, Strassburg, 1890, Verlag v. K. J. Trübner.

the firm of Merck & Co. then introduced a mixture of those dyes which he had found to be satisfactory into the trade, and designated the product as pyoctanin. Their blue pyoctanin is essentially a mixture of chemically pure methyl violet 6 B, dahlia, and benzoyl violet (bleu de Paris), while their yellow product is said to be chemically pure auramin.

As regards the manner in which the dyes in question were tested, Stilling and his co-worker, Wortmann, started from the assumption that any effect achieved in the case of the more "resistant" bacteria would warrant the inference that a similar effect might be expected in the case of those "nobler forms," which require special media for their successful cultivation. As I shall have occasion to show later on such a conclusion is totally unwarrantable. So far as Stilling's and Wortmann's work with pure cultures is concerned, they have established the fact that *staphylococcus aureus* does not develop in dextrose broth containing methyl violet (blue pyoctanin) in dilutions down to 1 to 1,000,000 and even of 1 to 2,000,000 (second communication, p. 21); that the typhoid bacillus succumbs in dilutions of 1 to 6000 in three hours; *Bacillus subtilis* in dilutions of 1 to 4000 in seventy-five minutes; *Bacillus anthracis* in dilutions of 1 to 16,000 in ten minutes; *subtilis* and anthrax spores in dilutions of 1 to 1,000,000 in twenty-four hours. Similar results were obtained with cultures of several moulds, such as *penicillium glaucum*, *phycomyces nitens*, and *aspergillus niger*. The remaining experiments were not conducted with pure cultures nor with other pathogenic organisms, but had reference merely to mixtures of the "common putrefactive organisms." As a result of their findings, Stilling concludes that in sufficient concentration the dyes in question will effectively prevent the development of practically all the different bacteria. Their mode of action Wortman explains as follows: When the organisms are first placed in the colored solutions the dye is deposited in the intermicellary spaces of the covering membrane, which is thereby stained. From these it can be extracted again by merely placing the cell in water. He adds that even without supposing that any chemical union has taken place, the mere occlusion of the intermicellary spaces would suffice to more or less seriously affect the metabolism of the cell and could thus lead to more or less serious consequences without actually causing death. On longer exposure or in the presence of a greater concentration of the dye a certain quantity of the latter may then be supposed to enter the protoplasm of the cell, where it may in turn exist as in the membrane, *i. e.*, physically absorbed in its intermicellary spaces, and from which it may be extracted again by placing the cell in water, as in the first instance. Regarding the manner in which the death of the organism is ultimately brought about, by further increasing the concentration of the dye or the period of time of its action, Stilling

assumes that in consequence of the increased storage "the vital movements of the plasmatic micellæ are arrested," death being the outcome. When this has occurred the dye can no longer be exhausted with water. Whether or not chemical union is responsible for this final result he leaves undecided.

Since intracellular metabolism is intimately connected with the action of the enzymes the question has naturally suggested itself whether the deleterious action of the dyes may not in part be referable to interference with the activity of these components. Stilling and Wortmann found as a matter of fact that this may be possible in an indirect way at least, but they have only touched upon this question in a casual way, so that definite conclusions are scarcely warrantable.

On the basis of his experimental studies, which were further extended by animal experiments, in which Stilling could demonstrate that the bacteria in question could actually be killed by the dyes, and that the "pyocyanin" is virtually non-poisonous, he enthusiastically recommended the substance for the treatment of minor surgical infections and advanced many instances to prove its beneficial effect. His therapeutic results were confirmed by several observers,⁸ while they were contradicted by others.⁹ To judge from the meagre literature one gains the impression as though the subject had been abandoned prematurely, as the laboratory data are certainly encouraging enough to warrant a more laborious investigation of the therapeutic possibilities of the subject.

Following Stilling's publications there are only incidental references to the bactericidal properties of aniline dyes recorded in the literature, the most interesting of which is the paper of Drigalski and Conradi.¹⁰ These writers eliminate the growth of associated acid forming cocci in their method of isolating the typhoid bacillus from the feces, by adding crystal violet, in a dilution of 1 to 100,000 to their medium, as they found that this dye possesses an *elective bactericidal action*, preventing the development of the cocci in question while not interfering with the growth of the typhoid bacillus. Systematic investigations of the selective action of crystal violet or other dyes are not recorded, however.

The first detailed investigations in this direction were made by Churchman, who confined his attention to a single dye, *i. e.*, to gentian violet it is true, but studied the action of this in reference to a large number of pathogenic and non-pathogenic organisms. As a result he divides the various microorganisms into violet positive and violet negative ones, meaning by violet positive that the growth of an

⁸ Sée and Moreau, *Médecine moderne*, July, 1890; Petersen, *Petersburger med. Woch.*, July, 1890; Jänicke, *Fortsch. d. Med.*, June 15, 1890. See also Stilling's second communication.

⁹ Garré and Troje, *Münch. med. Woch.*, 1890, No. 25.

¹⁰ *Zeitsch. f. Hygiene*, 1902, xxxix, 283.

organism is inhibited by the violet dye in question, and *vice versa*. The first group he found to include the *Bacillus subtilis*, *Micrococcus aureus* and *albus*, *Bacillus diphtheriæ*, *Bacillus anthracis*, *Sarcina rosea*, *Streptothrix actinomyces*, *Blastomyces*, and certain yeasts. The negative group includes the *Bacillus prodigiosus*, *Bacillus pyocyaneus*, *Bacillus typhosus*, *Bacillus paratyphosus*, *Bacillus lactis aërogenes*, and the *Bacillus suipestifer*. This behavior toward gentian violet Churchman found to be "so constant and clear-cut that it must be regarded as a fundamental biological characteristic. A few species have been encountered, like the streptococcus, an occasional strain of which varies in this respect; but for the vast majority of bacterial species and for the vast majority of bacterial strains the behavior toward gentian violet is almost, if not absolutely constant." In comparing the biological behavior of the different organisms toward gentian violet with the behavior of the same ones when studied according to Gram, Churchman was struck with a certain parallelism between the two phenomena. Of the 130 species which were investigated, he found 77 Gram-positive and 53 Gram-negative, and of the former 70 (or 90 per cent.) were violet positive, while of the latter only 8 (or 15 per cent.) were inhibited in their growth by the dye.

As regards Churchman's technique and many interesting details I must refer the reader to the original. At this place I would, however, emphasize that Churchman was able to distinguish a special strain of the *Bacillus enteritidis* from four other strains of the same group by its differing behavior toward gentian violet, while in all other respects the five strains were indistinguishable the one from the other.

In reference to the mode of action of the gentian violet, Churchman does not seem to have come to any definite conclusion. He points out that it does not depend on the presence of arsenic nor upon any change in the reaction of the media; presence or absence of light produces no difference, while the question whether or not the effect was due to any radiant properties of the dye could not receive an ultimate answer.

B. PERSONAL INVESTIGATIONS. For some time past I have had in view a systematic study of malignant growth by vital staining, but have thus far not been able to conduct it. Churchman's¹¹ interesting papers have revived this desire, but in view of the expense of the undertaking it seemed advisable to gain a closer insight into the selective action of aniline dyes upon simpler organisms first, and to study this more specifically from *the standpoint of structural chemistry*.

Technique. The technique which I employed was very simple. Nutrient agar was impregnated with the various dyes in the pro-

¹¹ Churchman, J. W., Jour. exper. méd., 1912, xvi, 221; Churchman, J. W., and Howard, M. V., *ibid.*, S22; Churchman, J. W., *ibid.*, 1913, xvii, 373.

portion of 1 to 100,000 and slants then inoculated with the different organisms and incubated for twenty-four hours. At the end of this time the results were noted; a three plus (+++) sign being used to indicate copious growth, double plus (++) fair growth, single plus (+) slight growth, plus over minus (+-) almost complete inhibition, and zero (o) absence of any growth. If at the end of twenty-four hours no growth was apparent the tube was returned to the incubator for another period of twenty-four hours; if there was still no growth apparent the surface was gently scraped with the platinum loop and a tube of plain agar, broth, or litmus milk inoculated, according to the nature of the organism. The result was not marked as negative unless the apparent absence of growth on the dye agar was thus controlled and confirmed.

The organisms studied were for the most part the ordinary ones which are pathogenic for man, different strains being procured especially of those which belonged to an apparently dye-positive group; they include the *Staphylococcus aureus*, *Micrococcus catarrhalis*, streptococci from different sources, the pneumococcus, the meningococcus, the *Bacillus typhosus*, paratyphosus *a* and *b*, paracoli and coli, the *Bacillus enteritidis*, the *Bacillus anthracis*, the *Streptothrix actinomyces*, the various strains of the *Bacillus dysenteriae*, and the cholera vibrio. In addition some of the more common non- or semipathogenic organisms were studied in reference to certain ones of the dyes such as the *Bacillus subtilis*, the *Micrococcus aurantiacus*, *Bacillus proteus*, *Bacillus acid lactis*, *Bacillus alkaligenes*, *Bacillus cholerae suum*, *Bacillus septicæmiæ hæmorrhagicæ*, and the *Bacillus prodigiosus*. The aniline dyes which were investigated include representatives of all the different groups. (See table in second communication.)

The Effect of the Color of the Dye in its Action on Bacteria. From the fact that Churchman divides bacteria into a violet-positive and violet-negative group, and that Stilling comprises all the different violet dyes under the heading of "methyl violet," one gains the impression that these observers attach a certain significance to the violet color of the dye so far as its inhibitory or bactericidal action is concerned. Table I, however, shows that the mere possession of a violet color on the part of an aniline dye does not necessarily carry with it a bactericidal effect, for we see from this that whereas crystal violet, methyl violet B, and dahlia may prevent the development of certain strains of staphylococci and streptococci, gallocyanin, roth violet 5RS, acid violet, and ponceau do not possess this property (in the standard concentration of 1 to 100,000).

TABLE I.

	Cryst. v.	Methyl v.	Dahlia.	Gallo.	Roth v.	Acid v.	Ponceau.
<i>Micrococcus aureus</i> (1) .	0	0	0	+++	+++	+++	+++
<i>Streptococcus anginae</i> (78)	0	0	0	+++	+++	+++	—
<i>Streptococcus anginae</i> (81)	0	0	—	+++	+++	+++	+++

The Effect of the Color of the Dye in Relation to its Acid or Basic Properties. Subsequent studies then showed that the color of the dye may be a factor in the production of the bactericidal effect, but only insofar as the acid or basic character of the substance is concerned. It will be recalled that this is dependent upon the presence of certain auxochromic groups, of which the amino group (NH_2) has basic properties, while the hydroxyl (OH), carboxyl (COOH), sulphonyl (SO_2OH), nitro (NO_2), and nitroso (NO) groups have acid properties. As is well known the basic dyes are for the most part of right spectral colors, viz., the various shades of violet and blue, while most of the acid dyes are left spectral in character, that is, red, orange, and yellow. Now we find as a matter of fact that those violet and blue dyes which are basic in character may be bactericidal in their action, while the acid red, orange, and yellow dyes do not possess this effect. (See Table II.)

TABLE II.

	Basic right spectral.			Acid left spectral.		
	Cryst. v.	Methyl v.	New methylene blue.	Rosindulin 2G.	Orange G.	Tartrazin (yellow).
<i>Micrococcus aureus</i> (1)	0	0	0	+++	+++	+++
<i>Streptococcus anginae</i> (78)	0	0	0	+++	+++	+++

Since there are exceptions, however, to the above rule regarding the interrelation between basicity and right spectral colors on the one hand and acidity and left spectral colors on the other, the question naturally suggests itself (1) whether a basic dye of left spectral color may not also possess bactericidal properties, and (2) whether an acid dye of right spectral color may not be capable of similar action.

TABLE III.—Basic Left Spectral Colors.

	Fuchsin.	Pheno-safranin.	Tolusafranin.	Azin red.	Rhodamin 3B.
<i>Micrococcus aureus</i> (1)	0	—	—	—	0
<i>Micrococcus aureus</i> (42)	0	—	—	—	0
<i>Streptococcus anginae</i> (54)	0	—	0	0	—
<i>Streptococcus anginae</i> (77)	—	0	0	0	—
<i>Streptococcus anginae</i> (78)	0	0	0	0	—
<i>Streptococcus anginae</i> (50)	0	—	—	0	0
<i>Bacillus anthracis</i> (14)	—	—	—	0	0

TABLE IV.—Acid Right Spectral Colors.

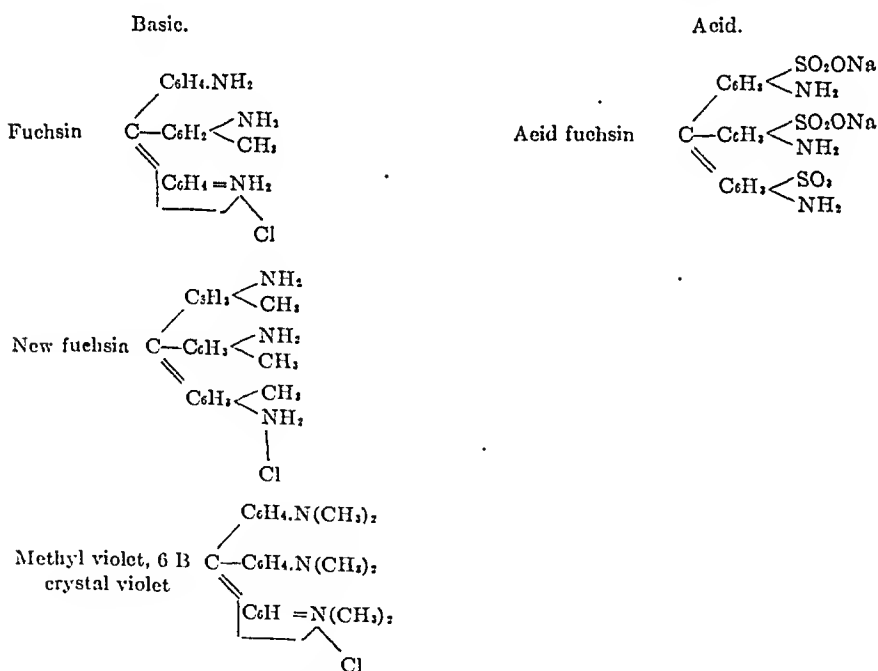
	Indulin R.	Acid violet.	Gallocy.	Uranin blue.	Acid alizarin.
<i>Micrococcus aureus</i> (1)	+++	+++	+++	+++	+++
<i>Streptococcus anginae</i> (85)	+++	—	—	+++	+++
<i>Streptococcus anginae</i> (92)	+++	—	—	+++	+++
<i>Streptococcus anginae</i> (50)	+++	+++	+++	+++	+++
<i>Bacillus anthracis</i> (14)	+++	+++	+++	+++	+++

Table III shows the relation of organisms which readily succumb to basic dyes of right spectral colors when tested against basic dyes of left spectral color, while the action of various blue and violet acid dyes is shown in Table IV. From the former it is apparent that there are basic red dyes which have bactericidal properties, while Table IV shows clearly that even though the color of a dye be blue or violet it does not follow that such a dye is bactericidal. As a matter of fact, I have not yet met with a dye of either pure or predominatingly acid properties which was bactericidal in character. Some dyes, it is true, have both acid and basic groups, but in the relatively few instances in which bactericidal tendencies were noted in substances of this order the basicity outweighed the acidity.

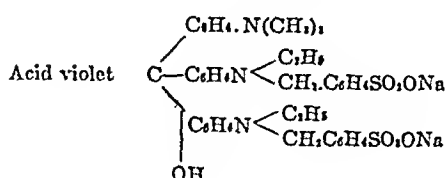
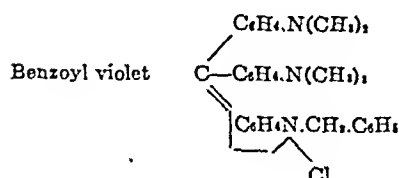
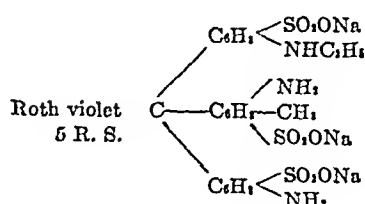
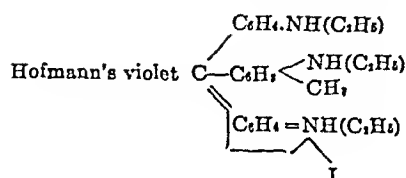
It may then be regarded as an established fact that *an acid dye irrespective of its color* (in the standard concentration of 1 to 100,000 at least) *is devoid of bactericidal properties, while a basic dye, likewise irrespective of its color, may possess inhibitory power.* I regard the elucidation of this fact as important in principle, as it seems to eliminate the possibility that the bactericidal action (in the concentration used) which certain dyes possess could be dependent exclusively upon physical influences. The size of the molecule more particularly could scarcely be an essential factor in the production of the bactericidal effect. In the case of methyl violet 6B (hexamethyl pararosanilin), which is markedly inhibitory, we thus find the molecule composed of 25 atoms of carbon, 30 of hydrogen, 3 of nitrogen, and 1 of chlorine, giving a molecular weight of 397. Amethyst violet, on the other hand, also a basic dye, is made up of 26 atoms of carbon, 31 of hydrogen, 4 of nitrogen, and 1 of chlorine, giving a weight of 414; in other words, it is but little larger than methyl violet and composed of the same elements, and nevertheless its bactericidal power is but very feeble. If, as Stilling suggests, this is essentially due to a closing up of the intermicellary spaces by the large molecules of the dye, then it would be difficult to understand why methyl violet should have a marked bactericidal power, and amethyst violet such of slight degree only, unless indeed it were argued that the latter molecule were too large. The difference between the two is so small, however, as to make this rather unlikely, but even if we were to admit this possibility for argument's sake, it would become invalid in view of the fact that Hoffmann's violet is just as strongly bactericidal as methyl violet, while its molecule is still larger than that of amethyst violet, being a triethyl homorosaniline iodohydrate, $C_{26}H_{32}N_3I$, corresponding to a molecular weight of 493. I have purposely compared methyl violet with amethyst violet, because both are made up of the same elements, and both are basic dyes, as the comparison with an acid dye, containing oxygen or oxygen and sulphur atoms, might be objected to on the basis of the dis-

similarity between the two groups in this respect. If, however, this were done it would become even more apparent that the size of the molecule has little if anything to do with the bactericidal effect, as we see it in such weak solutions as 1 to 100,000. While the basicity of the dye is thus an essential factor in determining its bactericidal power it does not follow that all basic dyes possess this property, and the question naturally arises whether there is still another factor in the structure of the dye which is of moment in this respect. When I first considered this question in connection with gentian violet the thought naturally suggested itself that the property might be referable to the underlying triphenyl methane group. A study in this direction showed, as a matter of fact, that it is common to all the red, blue, and violet triamino-triphenyl-methanes insofar at least as they are water soluble, and insofar as their basicity is not diminished through the introduction of acid auxochromic radicles.¹² If such radicles are introduced the inhibitory action is lost.

The basic and acid dyes belonging to this group which were studied in this direction, and their structural formulæ, are the following (arranged side by side, so as to show their interrelation):



¹² After my own work had been completed and in preparation for the press, Churchman published a third paper on the subject in question, in which he states that he thought it wise to attack the problem by studying substances closely allied to gentian violet in chemical structure, and found that dahlia parafuchsin, magenta, pararosanilin, rosanilin, crystal violet, and methyl violet 5B inhibit the growth of the anthrax bacillus and *Micrococcus aureus*, while they are of no effect upon the development of the colon and the typhoid bacillus (the only four organisms studied in this direction). He adds that the determination of the chemical group responsible for the bactericidal action of these dyes is the subject of investigations now under way at the laboratory of surgery at Yale University.



Dahlia (a mixture of methyl violet and fuchsin.)

The effect of these dyes upon some of the organisms which are of special interest in this question, and the difference in the behavior of the acid as compared with the basic representatives is shown in the following table:

TABLE V.—Showing Inhibitory Effect of Acid Representatives of the Triamino-triphenyl Methane Group (Red, Blue, and Violet Colors).

	Micrococcus aureus (1).	Strepto- coccus (85).	Micrococcus catarrhalis (6).	Bacillus subtilis (4).	Bacillus anthracis (14).	Actino- myces (15).
Basic:						
Fuchsin	0	0	0	0	0	0
New fuchsin	0	0	0	—	0	0
Methyl violet	0	0	0	0	0	0
Crystal violet	0	0	0	0	0	0
Hofmann's violet	0	0	0	0	0	0
Benzoyl violet	0	0	0	—	0	0
Dahlia	0	0	0	0	0	0

Acid:

Acid fuchsin	+++	+++	+++	+++	+++	+++
Roth violet	+++	+++	+++	+++	+++	+++
Acid violet	+++	+++	+++	+++	+++	+++

The green basic triamino-triphenyl-methanes are not as uniformly inhibitory as the red, violet, and blue. Of the three which were studied, iodine green is an iodomethylated methyl violet, methyl green, a corresponding chlormethylated product, and ethyl green a bromomethylated hexaethyl pararosanilin. All three are triphenyl methanes and all three are basic, but notwithstanding this fact only one, that is, ethyl green, has well-developed inhibitory properties. This difference is no doubt due to the fact that the second dimethylamino group is transformed into an ammonium base by the halogen alkyls, and that the basicity of the compound is thereby lessened.

It may be interesting to point out that here also the introduction of acid auxochromic radicles leads to the disappearance of any

inhibitory action that the corresponding basic dyes may possess. The structural formulæ of the dyes in question and the differences in action are shown below (Table VI).

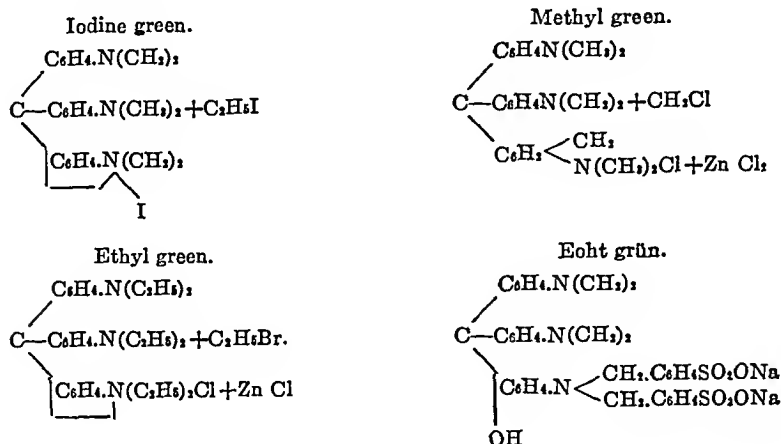
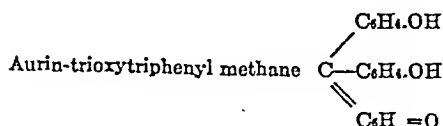


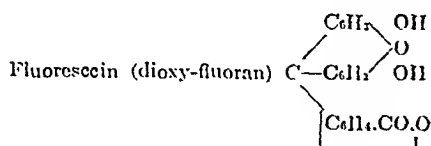
TABLE VI.—Table Showing the Varying Action of the Green Triamino-triphenyl Methanes.

	Iodine green.	Basic. Methyl green.	Ethyl green.	Acid. Echt grün.
<i>Micrococcus aureus</i> (1) . . .	+++	≈ to +	0	+++
<i>Streptococcus</i> (92) . . .	+++	+++	0	+++
<i>Micrococcus catarrhalis</i> (6) .	+	≈ to +	+	+++
<i>Bacillus subtilis</i> (4) . . .	+++	0	—	+++
<i>Bacillus anthracis</i> (14) . . .	+++	+++	0	+++
<i>Actinomyces</i> (15) . . .	+++	+	0	+++

Whether or not some alkyls produce a more marked inhibitory effect than others remains to be seen. Working with uniform concentrations of 1 to 100,000, I cannot say that I could note any essential difference between methylated, ethylated, and benzoylated compounds, unless indeed the relatively more marked inhibitory effect of ethyl green as compared with methyl and iodine green were regarded as evidence of such a difference. The essential factors in any event are not the alkyl groups, but the underlying triphenyl methane group in combination with the three strongly auxochromic amino groups. The importance of the latter has already been illustrated in various ways above, but is further emphasized in Table VII, in which it will be seen that the replacement of the amino by acid hydroxyl or hydroxyl and carboxyl groups leads to a complete suspension of an inhibitory effect. The dyes in question are representatives of the rosolic acid and the phthalein series. Their structural formulæ follow:



Corallin—constitutional formula not definitely known; probably an intermediary product between aurin and pararosanilin, in which both hydroxyl and amino groups are present..



Uranin—the potassium salt of fluorescein.



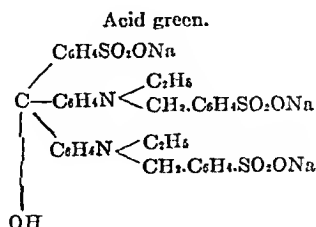
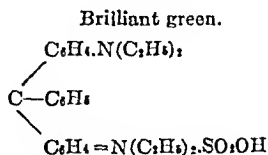
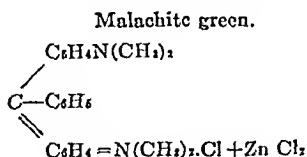
Erythrosin—the corresponding iodine compound.

The effect of these dyes upon some of the organisms which ordinarily are inhibited by the triphenyl methane dyes of basic character is here shown.

TABLE VII

	Corallin.	Uranin.	Eosin.	Erythrosin.	Aurin.
Micrococcus aureus (1) . . .	+++	+++	+++	+++	+++
Streptococcus (31) . . .	+++	+++	+++	+++	+++
Micrococcus catarrhalis (6) . . .	+++	+++	+++	+++	+++
Bacillus anthracis (14) . . .	+++	+++	+++	+++	+++
Actinomyces (15) . . .	+++	+++	+++	+++	+++

The diamino-triphenyl methanes occupy a position which is analogous to that of the green triamino-triphenyl methanes. Like these they are green dyes. I have pointed out that in the latter one amino group has been transformed into an ammonium base, the consequence being that they are virtually diamino compounds. The representatives of this order which were studied are the two basic dyes, malachite green and brilliant green, and the acid Säuregrün S. The formulæ are the following:



Here also as in the case of the triamino dyes the ethyl compound seems to possess a greater inhibitory effect than the corresponding methyl compound, which very curiously is largely directed against the streptococcus group. (See Table VII.) But the general inhibitory effect is evidently less than in the case of the red, violet, and blue triamino dyes.

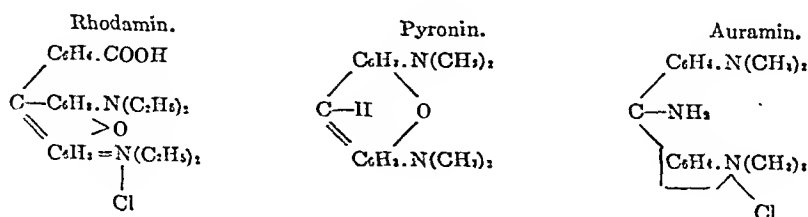
TABLE VIII.

	Basic.		Acid.
	Malachite green.	Brilliant green.	Acid green.
<i>Micrococcus aureus</i> (1)	+++	+++	+++
<i>Streptococcus</i> (50)	0	0	+++
<i>Streptococcus</i> (82)	++	0	+++
<i>Micrococcus catarrhalis</i> (6)	+++	++	+++
<i>Bacillus anthracis</i> (14)	0 to ±	+++	+++
<i>Actinomyces</i> (15)	0 to ±	+	+++

Standing midway between the phthaleins and the triamino triphenyl methanes are the pyronins, of which rhodamin B and pyronin G were studied. A glance at the formulæ of these bodies will show that they contain two amino groups, and an oxygen atom, replacing one hydrogen atom in two of the phenyl groups, but that rhodamin is a triphenyl product while pyronin contains but two phenyl groups. Rhodamin, moreover, contains a carboxyl group in combination with one of its phenyl groups. As the basicity of one amino group outweighs the acidity of one carboxyl group, we may view rhodamin essentially as a basic dye of the triphenyl methane type, and as such we find that it possesses inhibitory properties, which, however, are not as extensive as those of the triamino products. Pyronin, on the other hand, though markedly basic in character, has no inhibitory action in the concentration which we have chosen as our standard, and the question hence suggests itself whether this may not be owing to the absence of the third phenyl group. The behavior of the single representative of the diphenyl methanes which I have studied, namely, auramin O, suggests that this may indeed be the explanation, though it does not follow that every diphenyl diamino dye should behave in a similar manner. All that we wish to say is that diamino diphenyl products of methane origin do not possess inhibitory properties in the concentration of 1 to 100,000.

The formulæ of the substances just referred to and their effects upon the organisms in question follow:

TABLE IX.



	Rhodamin.	Pyronin.	Auramin.
<i>Micrococcus aureus</i> (1)	0	+++	+++
<i>Streptococcus</i> (92)	+++	+++	+++
<i>Micrococcus catarrhalis</i> (6)	0	+++	+++
<i>Bacillus anthracis</i> (14)	0 to \pm	+++	+++
<i>Actinomyces</i> (15)	0 to \pm	+++	+++

SUMMARY. 1. The inhibitory effect which certain violet dyes, like gentian violet, methyl violet, dahlia, etc., exercise upon certain bacteria is not referable to their violet color, but to their chemical structure as triamino triphenyl methanes, and is intimately dependent upon their basic auxochromic groups.

2. Acid dyes irrespective of their chemical structure and color, do not possess this inhibitory power.

TYPHLO-ALBUMINURIA.¹

BY HEINRICH STERN, M.D.,

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It is not rare to find a clinician assigning an alimentary origin to a case of albuminuria when it cannot be attributed to an existing kidney disease and when the albuminuric phenomenon follows the ingestion of generous amounts of meat, cheese, milk, gelatin, or raw egg albumen. While it is true that in persons with faultless kidneys the ingestion of the raw whites of three or four eggs may result in the excretion of the unchanged ovalbumin, very little, indeed, is known of the albuminurias supposedly occurring in the wake of an overplus of the other protein foodstuffs. In such albuminurias only serins—serum albumin together with serum globulin or serum albumin alone—and no blood-foreign protein are excreted by the urine.

It is for this reason that, apart from ovalbuminuria occasionally following the intake of excessive amounts of raw egg albumen, no definite connection between protein ingestion and the urinary albumin has as yet been established. Every food protein is altered prior to absorption, and though its end-products will ultimately reach the renal secretion, it will not therein reappear in its native physicochemical formation.

There is, moreover, no probability that such a relationship can ever be positively demonstrated so long as we hold to the belief that the protein substance designated by us as serum albumin must have formed a constituent part of the blood. This assumption not only presupposes that the living organism exhibits its contents

¹ Read at the Annual Meeting of the Medical Society of the State of New York at Rochester, April 30, 1913.

of serum albumin exclusively in the blood plasma, but also that the escape to this protein from the body must ensue by way of the kidneys.

The albumin of the lymph, however, is entirely identical with serum albumin. Inasmuch as we cannot differentiate one from the other, we would be unable to recognize the source of albumin appearing in the urine were it not for the facts that globinuria is a conspicuous concomitant of serum albuminuria while it is decidedly less manifest or entirely absent in lymphuria, and that the latter usually shows considerable numbers of lymphocytes on subjecting a sediment to microscopic examination.

If we accept the fact that albumin may be transmitted to the urinary fluid by traversing the lymph channels—and I have furnished sufficient evidence that this may be the case—² then it is even possible that the well-developed network of renal lymphatics need not play any role whatever in this process, for the lymph albumin may enter the urinary tract by way of the lymph-paths leading to the ureters and the bladder. The superficial ureteral and vesical lymph vessels directly adjoin the upper epithelial layer of the mucosa communicating with it, and thus a portion of their lymph content may under certain conditions exude into the lumen of the ureter and the interior of the bladder.

In alimentary albuminuria in general and typhlo-albuminuria in particular there is one main channel, and in uncomplicated cases it is probably the only one, through which the protein is conveyed to the urine—the lymphatics. It is the route taken by the chyle in the condition known as chyluria, and a similar if not the same one often followed by the colon bacillus invading the urinary tract when the infection is not of the ascending type. Nevertheless, I am not as yet prepared to positively state whether or not alimentary albuminuria is a true lymphuria, for one of the characteristic features of this, the presence of large numbers of lymphocytes, is generally wanting. At the same time there ensues no or but an inconsiderable globulin excretion in the albuminurias of intestinal origin. This latter factor at once precludes the blood as the protein carrier in these types of albuminuria.

It might be possible that the criteria of lymphuria as advanced by me are too stringent, and that this condition may exist even when the urine does not show considerable numbers of lymphocytes that are not the result or the accompaniment of destructive processes. Assuming, then, that this be the case, an alimentary albuminuria would be a lymphuria—an assumption which is so much more plausible than that which tries to trace the urinary albumin back to the blood current.

² Heinrich Stern, *Lymphuria and its Clinical Status* (Arch. Diag., April, 1913), *The Clinical Evidence of Lymphuria* (Med. Rec., May 31, 1913), and *Ueber Lymphurie und ihren klinischen Status* (Berl. klin. Woch., October 13, 1913).

Typhlo-albuminuria is an alimentary albuminuria proceeding from the cecum. It is probably the most frequent of all the intestinal albuminurias. It has a recidivating character, that is, it disappears and returns at irregular intervals, and seems to ensue quite independently from the protein intake just preceding it. It may be continuous for several days and again be absent for weeks at a time. Typhlo-albuminuria invariably occurs in persons with habitual constipation, which latter appears to stand in more or less etiological connection with it. Its immediate causative factors are probably analogous to those permitting the transmigration of the colon bacillus from the cecum to the renal pelvis, ureter, or bladder and terminating in colipyelocystitis. These pathogenic factors are cecal atony, the absorption of nearly or all the liquid from the cecum, the resulting extreme dryness of the feces, and coprostasis. At any rate, we cannot speak of a typhlo-albuminuria unless the cecum appears to be at the bottom of the albuminuric phenomenon. The latter may supervene during or after a paroxysm of severe griping pain in the cecum (oftentimes a characteristic of cecal atony), but it is more frequent in those instances of typhlatonia in which there is no definite paroxysm of pain, but constant discomfort due to fulness, compression, or traction at the site of the cecum. While it is now a comparatively easy matter to recognize typhlatonia and to differentiate it from chronic appendicitis³ the appendix itself may be adherent to the cecum and thus occasion or aggravate the latter's atonic state.

The structurally or functionally defective cecum is bound to more or less disturb the intra-abdominal equilibrium in general and the visceral lymphatics in particular. The latter, including those of the cecum itself and its mesocolon, become readily over-filled and a lymph stasis may ensue which in itself may give rise to abdominal and lumbar discomfort. The escape of some of the contents of the engorged lymph channels through newly formed lymph varices near the surface of the lining epithelium of the urinary tract is but a natural consequence. Whenever an anastomosis between the cecal or mesenteric lymphatics on the one hand, and those of the urinary apparatus on the other, is effected, the albuminuric phenomenon may even ensue in the absence of any considerable cecal disturbance, and the typhlo-albuminuria may thus attain a certain degree of chronicity.

The occurrence of typhlo-albuminuria does not seem to depend so much upon the amount of protein ingested at any one time as on the interrupted draining of the lymph stream into the venous system. There is set up a localized lymph stasis resulting in the absolute augmentation of lymph albumin. While no albumin can be detected in the urine immediately before the lymph paths

³ Heinrich Stern, *Atony of the Cecum: A Procedure Facilitating its Recognition*, Arch. Diag., October, 1912, and *Atony of the Cecum (Typhlatonia)*, Arch. Diag., January, 1913).

communicate with any of the lumina of the urinary apparatus, it will be found by the ordinary clinical methods as soon as the anastomosis has become patent. It is this sudden appearance of urinary albumin which has given cause to the unjustified assumption (excepting the circumstance of the ovalbumin) contending that this type of albuminuria is the direct consequence of the increased ingestion of protein material.

Besides an albuminuria, a visceral lymph stasis may engender other clinical phenomena. There exists, for instance, an albuminoglycosuria which is of lymphatic origin, and which I shall describe in detail as soon as I have collected all my necessary data.

In 2 of my 4 cases of true lymphuria⁴ I have encountered traces of fatty material on the surface of the urine upon standing for some time. I have not as yet observed any urinary fat excretion in cases of typhlo-albuminuria or alimentary albuminuria in general, but it must be known that my investigation of these particular types of albuminuria were not begun before May, 1912, and that the material at my disposal was limited to 10 cases, namely, 5 of typhlo-albuminuria and 5 in which the direct cause of the albumin excretion was evidently located in another segment of the colon; 2 of the latter cases were associated with a glycosuria.

Theoretically reasoning, typhlo-albuminuria ought to be a unilateral, that is, a right-sided albuminuria. There is not only the close proximity of the cecum to the right half of the urinary apparatus and the bladder (I recall the substitution of the cecum for the resected bladder by P. Lengemann,⁵ but also the intimate lymphatic communication between these organs. To my regret in but one of my cases was I permitted to obtain the separate urine from each kidney by ureteral catheterization. In this case, which is reported in the following, the albuminuria proved to be bilateral, though its intensity degree was from three to four times larger in the secretion from the right than in that derived from the left ureter.

CASE.—Male, aged thirty-two years; well-developed. No history of scarlatina or diphtheria. Gonorrheal infection ten years before. Six years before was accepted by a life insurance company, but the previous year was rejected by the same and two other insurance companies on account of albumin in his urine. Has since been under treatment by his family physician, without avail, however, as far as the albuminuria is concerned. This was irregularly intermittent; it was present for a few days in succession at all hours of the day; at other times it would be found between 3 o'clock in the afternoon and bedtime; and again at other times it would not appear for some days. Complaints of fulness and dragging in the right side of the abdomen, occasional sharp pains,

⁴ Arch. Diag., April, 1913.

⁵ Zentralbl. f. Chir., 1912, No. 50.

lasting for from half an hour to an hour and a half, in the right inguinal region; constipation and hemorrhoids. There was no heart or appreciable bloodvessel disease; the pressure over both radial arteries was 140 mm. Hg. The neurological findings were negative. The twenty-four hours' urinary output fluctuated between 1400 and 1800 c.c. The specific gravity varied between 1023 and 1026. The urine was invariably of a normal acid degree. The albuminous urine never contained globulin. The epithelia distinguished came mostly from the upper layers of the ureters, bladder, and urethra. Besides there were some prostatic epithelia. The few leukocytes encountered were well granulated and of good constitution. In addition there was a limited number of small-calibered calcium oxalate crystals. No renal formed elements or tube-casts were found in the numerous urine specimens submitted to microscopic examination. The separate urines obtained by ureteral catheterization evidenced bilateral albumin excretion; however, the urine from the right ureter contained three or four times as much protein as the one obtained from the left ureter. The test for the functional activity of the kidneys with phloridzin, of which 1 cm. (0.01) was injected hypodermically, showed the excellent working powers of these organs, as their secreting epithelium produces not less than 8.63 grams glucose, that is, about six times more than is furnished by kidneys yet considered physiologically efficient.

The abdominal organs appeared normal, with the exception of the ascending colon and the cecum, which were both distended, the former by gases and the latter by liquid, and apparently also by solid material. There was considerable pressure sensitiveness over the cecum, which was readily mapped out and demarcated from the ascending colon by pereussion. Arising from within it there were distinct gurgling sounds. Stern's procedure confirmed the diagnosis of cecal atony.

The albuminuria in this case was entirely independent from the protein intake. It was even more intense on the days the patient reduced the total food intake and abstained entirely from animal proteins. The enhanced intensity degree of the albuminuria continued sometimes on the following day.

A mixed diet rich in cellulose, the imbibing of not less than two liters of water per day, regulated bodily exercise, and the wearing of a cecal support afforded cecal relief, and also lessened the albuminuria days and the absolute output of albumin.

Our knowledge about alimentary albuminuria is very meager, and the few conceptions we entertain concerning it are in need of a thorough revision. An alimentary albuminuria in the first instance should not so much signify the excretion of ingested albumin as the egestion of proteid material due to some anomaly of the alimentary tract. Typhlo-albuminuria is a true alimentary albuminuria in which the sequence of cause and effect can clinically be demonstrated with certainty in well-nigh every instance.

THE METABOLISM, PREVENTION, AND SUCCESSFUL TREATMENT OF RHEUMATOID ARTHRITIS: SECOND CONTRIBUTION.

BY RALPH PEMBERTON, M.S., M.D.,

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(Continued from January, 1914.)

CASE XI.—Mrs. R., aged forty years, white. Referred by Dr. Frank Dickson. The patient gave a history of having had when aged sixteen years an attack of rheumatism, in which several joints became swollen, red, and painful. She recovered in three or four weeks, though afterward she had at times some discomfort of the same general nature in her ankles and knees especially, lasting for a day or two. Three and a half years previously, pain affected her ankles more severely, followed in two to three months by involvement of her knees. The thighs became flexed, and in a few months more the hands and elbows were affected, the latter becoming little by little "locked" in partial flexion.

Her first medication consisted of ten bottles of patent medicine, after which she was treated by a physician for three months, and received electricity at the Medico-Chirurgical Hospital. She grew worse and next tried homeopathy for ten weeks at the West Philadelphia Homeopathic Hospital, without benefit. She was then treated for two years by an osteopath, who used hot packs and massage, and was finally referred to the Hospital of the University of Pennsylvania in the summer of 1912, where she spent ten weeks. While there her knees were straightened by bed weights. Shortly after her discharge from the hospital her hands grew worse, and she lost all use of them.

For one year past she has been troubled with belching, and occasionally with pain in her stomach, nausea, vomiting, and flatulence. Apart from her arthritic state, she presented but one gross abnormality, and that was a profuse leucorrhea, smears from which showed an intra- and extracellular, Gram-negative diplococcus, apparently Neisserian. This discharge was of two years' duration.

Examination by Dr. George E. Shoemaker showed chronic vaginitis and vulvitis, but little or no pelvic involvement.

In regard to her joints, she presented nearly the condition of the so-called "ossified man." She lay almost without motion in bed, with her left hand over her left flank and her right upon her epigastrium. She could not move her knees, which were in extension; her feet and toes were barely movable, her left elbow was

not at all movable, and the right allowed only a slow painful change from mid- to full flexion. The left hand was subluxated on the wrist; the fingers of both hands could barely be moved, some not at all, and all were in varying degrees and positions of flexion and extension, one terminal phalanx being acutely extended dorsally to 45 degrees. She could not put either hand to her head, could not change her position in bed in the slightest, could not feed herself, and so great was the involvement of her jaws that they could not be separated more than enough to admit a spoon. Her hips and spine still permitted some motion, and her head was quite freely movable in all directions. Both knees were greatly enlarged; the skin of the legs was very glossy, and the thighs could be but slightly abducted; but nowhere was there much soft tissue swelling.

Her blood-pressure was 115 systolic and 90 diastolic; bowels were costive; urine showed large numbers of white blood cells, but no casts, and gave indican reactions varying between negative and very large amount. Blood examination showed red-blood cells, 4,580,000; white-blood cells, 10,050; hemoglobin, 60 per cent.

Examination of the ears, nose, and throat by Dr. N. P. Stauffer, showed a general low-grade inflammation characteristic of so-called rheumatic sore throat.

The x-ray examination revealed the bowel to be in normal position and not elongated. The radiograph was taken in the prone position, however, as the patient could not stand so that the evidence as to ptosis and kinking was not complete. There was clearly no elongation however. The hands showed great rarefaction of the heads of the bones, with predominance of the atrophic type of arthritis though decided hypertrophy was also present. The knees also showed widespread involvement with thickening of the lateral ligaments.

The patient was placed upon the house diet and the amount of food eaten was measured and, when necessary, weighed for several weeks.

Calculation of the caloric value of the food ingested on a sample day taken from this period gave a value of 1187 calories, though the intake was of course not constant and sometimes ran higher. This was a low intake of food, but was sufficient to maintain the patient on a high plane of nutrition, probably because her enforced immobility required but a small consumption of heat units, though she was a large and moderately stout woman. The figures above cited show an intake of only 10 calories, on the average, per pound of body weight, or about 22 calories per kilo body weight.

On April 12, 1913, she was placed upon the following diet, which yielded about 1009 calories. At her then body weight of 117.5 pounds, this gave about 8.6 calories per pound body weight or 19 calories per kilo of body weight.

It should be noted that before beginning treatment, efforts were made to cure the vaginitis, in the belief that it might be a contributing or causal source of her trouble, and she was given douches of potassium permanganate and other treatment to that end. After some weeks there was no marked response, however, and it was decided to attempt metabolic measures in the face of this known source of infection.

In point of fact the leucorrhea persisted during her entire stay in the hospital. Comment on this point will be made later.

From experience in the cases heretofore cited, from laboratory data in regard to the ethereal sulphates, and from other suggestive observations, it seemed reasonably clear that proteids could be tolerated by these cases in relatively large amounts, and that the carbohydrates were at least jointly to blame in contributing to the disease.

To what degree the carbohydrates could be tolerated, however, was not so clear, and the present case was deemed a suitable one to be placed upon a diet high in carbohydrate and low in proteid, relative to the total calories, as follows:

Breakfast: 1 cup of weak coffee, with 1 tablespoonful of cream and $\frac{1}{2}$ teaspoonful of sugar; butter, 5 grams; rice, 50 grams with $\frac{1}{2}$ teaspoonful of sugar; toast, 30 grams.

Dinner: Baked potato, 150 grams; butter, 5 grams; toast, 30 grams; 1 cup of weak tea, with 1 tablespoonful of cream and 1 teaspoonful of sugar; stewed tomatoes, 3 tablespoonfuls.

Supper: Toast, 30 grams; butter, 5 grams; 1 cup of weak tea with 1 tablespoonful of cream; lettuce, with 1 tablespoonful of French dressing (2 parts of oil and 1 part of vinegar).

At dinner she was given an option of stewed celery (cooked without flour), spinach, or tomatoes. At all meals and between she had water and salt *ad libitum*. The proteid element in this diet was inconsiderable, while the carbohydrate and fat elements provided practically all the calories.

The notes recording her progress can profitably be introduced here:

April 15. Three days after diet started. There was a slight indication of improvement in her hands.

April 16. Patient insisted that there was an improvement in her hands, and that it had been greater in the past four days than in the previous twenty-six days since she had been in the hospital.

April 18. Improvement continued. Skin of forearms was shiny, as though tense, but had now lost its luster, and was showing minute wrinkles everywhere. There never was any obvious swelling of forearm proper, however. She turned better in bed, and could reach her arms across her body.

The patient did so well on this diet that it was thought of interest to reverse the conditions of her dietary, replacing the

carbohydrate largely by proteid, while keeping the total calories about the same. She was therefore given the following:

Breakfast: 1 cup of weak tea, with 1 tablespoonful of cream and 1 teaspoonful of sugar; 1 soft-boiled egg, 50 grams; butter, 5 grams; milk, f5vj, 1 glass.

Dinner: 1 soft-cooked egg, 50 grams; butter, 5 grams; tea as above; 3 tablespoonfuls of eelery stewed without milk or flour; 3 tablespoonfuls of tomatoes; lettuce, with 2 tablespoonfuls of olive oil and 1 tablespoonful of vinegar.

Supper: 1 soft-cooked egg, 50 grams; butter, 5 grams; tea as above; 3 tablespoonfuls of spinaeh; 3 tablespoonfuls of tomatoes; lettuce, with f5viij olive oil, and vinegar, f5j.

Through an error in administering the diet, the patient received twice the amount of oil intended, which raised the calories by 242, so that the total caloric value was 1212 instead of 970 as ordered. Nevertheless, she did well upon it, as far as her joints were concerned, as illustrated by the notes.

April 29. Diet changed the afternoon of the day before to a high proteid one. Patient enjoyed her meals fairly well and felt well. Held the newspaper and turned it for first time in ten months. For about five days had been able to touch her right hand to her head, which she could not do previously for eight months.

April 30. Improving, though on a proteid diet. Satisfied with it. More motion, especially in the fingers.

May 2. Improvement marked on the new diet. The vaginal discharge continued. Patient complained much of eructation, and said she received too many green vegetables. Curtailed them somewhat to patient's option. Motion increased in feet, hands, arms, jaws, and shoulders. Could reach the back of her head with right hand.

May 3. Feeling better. Nauseated at supper and ate less of lettuce, etc., than usual. Still improving. Liked other diet better, and had more appetite when taking it.

May 4. Doing well, but had to force her food. Changed to old carbohydrate diet.

May 8. Had no indigestion or nausea on carbohydrate diet. Did well on it. Appetite better.

May 10. No indigestion or nausea. Moved much better in bed. Fingers changing shape. Slight gain in weight. Vaginal discharge was considerable and still persisted. Got daily potassium permanganate douche of 1 to 2000, just as she had for six weeks. Could open her mouth wider. Wrote her name the first time since September.

May 30. Sat up in bed and fed herself for the first time.

June 10. Improvement continued steadily.

June 28. Evidence of arthritis proper had disappeared. Patient was suffering from tendinous contractures, partial ankyloses, and muscular atrophy of disuse. On October 6 improvement was still maintained.

CASE XII.—Miss M. G., aged thirty-six years, white. Referred by Dr. J. Edwin Sweet. The patient said that her mother had been similarly troubled for the last seven years of her life, dying at the age of sixty-three years, and that the present condition of the patient had begun seven years previous to admission. The first intimation of it was pain in one foot, which progressed after one year to the knees. Three years later the first metacarpophalangeal joints of the hands became involved, whence, during the ensuing year, the trouble spread to the shoulders, elbows, and wrists. Next the hands were more widely affected, together with the neck, to a milder degree, and finally both feet. Prior to the onset of the present trouble the patient's health had been good, and she gave no history of purulent infection anywhere.

The history of her various treatments as obtained from the patient is interesting, as illustrative of their failure and of the great variety undertaken. She was treated at her home in central New York for eighteen months without relief, after which she went to New York City, and was treated for five months on a diet of 1 quart of sour milk for breakfast, a lunch of vegetables (any kind), fruit, cereals, and cream. No sweets nor meat. Supper, 1 quart of sour milk. No relief followed this. Then she began taking aspirin, which she took for six months, after which she went to Mt. Clements, Michigan, and was treated for two months with forty-two baths and massage. She was much weakened after thirty-one baths, but kept on with the addition of more massage. She went home for five months under no treatment except aspirin, after which she went back to Mt. Clements for five weeks and had twenty-one baths, and osteopathy every other day. No improvement followed, and she returned to New York City, getting osteopathy every other day for three months. She then went to St. Luke's Hospital, New York, where she remained twenty-five months without leaving the hospital but obtained only slight relief. She was treated at various times by every conceivable therapy, including vaccines given over eight months.

On leaving St. Luke's Hospital she went to her home, whence she was referred by Dr. Sweet to the writer. While home, during the year following her stay at St. Luke's Hospital, she took large quantities of aspirin, sometimes as much as 60 grains a day, until her digestion became impaired, and she was advised to discontinue it.

Physical examination revealed an unusually frail and small woman of fair nutrition. There were no gross deformities, though the knees were slightly enlarged and could not be fully flexed or straightened. The metacarpophalangeal articulations of the hands

were thicker than normal, especially the first and second, and all the fingers showed ulnar deviation. The ankles were stiffened and sore. On both ulnæ, near the olecranon, were localized swellings the size of a strawberry, hard to the touch and apparently attached to the bone. There was no great soft tissue swelling anywhere. The teeth were good and well cared for, and an examination of the eyes by Dr. H. M. Langdon showed them to be normal, except for astigmatism. Examination of the nose and throat by Dr. N. P. Stauffer showed: "Deviation of septum of perpendicular plate of ethmoid; slight hypertrophy of the tonsils, the symptoms being those of chronic tonsillitis, with adhesions to the pillars. Moderate hypertrophy of turbinal bones. Membrana tympani slightly retracted and lacking usual luster. The picture is one of a chronic middle-ear disease (catarrhal) originating in the nares."

There was no apparent focus of infection elsewhere. The urine was normal and gave persistently no indican reaction. Blood examination showed red blood cells, 3,230,000; white blood cells, 9050; hemoglobin, 55 per cent.

X-ray examination showed the stomach to be much enlarged and the colon to be elongated, but the respective positions of the two organs were not well revealed, as the patient could not stand. The joints and bones showed both atrophic and hypertrophic arthritis, with a tendency more toward the atrophic variety.

Upon admission to the Presbyterian Hospital she was placed upon the regular house diet while certain observations were made, and an accurate record was kept of what she ate, so that her daily caloric intake could be approximated. The average of two days thus calculated showed a minimum intake of 1375 calories, which was 16.6 calories per pound of body weight or 37 calories per kilo. She was then placed upon a diet largely of carbohydrate and low in proteid, for the purposes mentioned in the last case, the total calories amounting to about 1156, distributed as follows:

Breakfast: 1 apple; 2 teaspoonfuls of coffee in 1 cup of hot water, with 1 tablespoonful of 20 per cent. cream, and 1 teaspoonful of sugar; 1 slice of toast, 30 grams; butter, 10 grams; boiled rice, 50 grams; salt and water *ad libitum* at and between all meals.

Dinner: 1 roasted potato, 150 grams; butter, 10 grams; 1 slice of toast, 30 grams; 2 teaspoonfuls of tea, with 1 tablespoonful of 20 per cent. cream, and 1 teaspoonful of sugar; option of tomatoes, spinach, or celery, stewed without flour.

Supper: 2 teaspoonfuls of tea in 1 cup of hot water, with 1 tablespoonful of 20 per cent. cream, and 1 teaspoonful of sugar, 1 slice of toast, 30 grams; butter, 10 grams; lettuce, with 1 tablespoonful of mixed French dressing (3 parts of oil to 1 of vinegar).

Her progress can best be illustrated by the daily notes:

April 26, 1913. Diet started April 19, P.M., and improvement was first noted on April 22, when it was evident that the hands

could be closed somewhat passively, with less pain to the patient. This continued until the above date, when for the first time in two years (patient says she is sure) she put a hairpin in with her left hand. On April 24 a ring came off of the third finger of the right hand that the patient could not remove when she entered the hospital, in accordance with the general rule that all jewelry must be put away. The ring had been on steadily for three years, and could not be removed. She could flex both knees slightly more and did so more quickly. Skin was slightly wrinkled over the knees and gloss growing less.

April 28. Always had pain and stiffening before, and for the first day or two of her menstrual period. Period began the day before, but she did not have an increase of pain and stiffness, and they both grew less. To test the effect of the hydrocarbons, 250 calories (about) of fat were to be added to her diet to bring it up to where it was in calories before treatment began; 15 grams of butter and 2 tablespoonfuls of olive oil were added daily. Lettuce and vinegar were added at supper, as a vehicle for the oil in the form of French dressing. Total calories were about 1507.

April 29. Had extra oil at supper. Felt more pain in joints, though motion was free. Day was raw and rainy, the patient was in the second day of her period.

May 2. Patient improved steadily since getting extra fat and oil, though she complained of indigestion from potato. Not hungry. For three days received by mistake 150 grams of potato opened out instead of weighed to that weight in the skin. She was ordered to revert back to 150 grams of potato weighed in the skin. Her caloric intake was therefore higher than was calculated, about 1604 calories, though made up considerably of fat. Knees unquestionably showed more bony points and more wrinkling of the skin over them.

May 3. Better as to nausea. Joints were improved. The purpose of the test was incompletely accomplished.

May 4. Nausea gone but she had some eructation at night. Could move her knees better and faster. Bony points were more prominent. Thought her fingers were stiffer, and that she was not quite so well as on the previous day. Was ordered to revert to old diet. She had a headache and was ordered aspirin and acetphenetidin for three doses only.

May 11. Much better in every joint. Could move her knees and shoulders better than at any time yet. Had much indigestion. also headache. One cascara pill ordered at night.

May 12. Complained of indigestion and pain from gas, etc. Butter was reduced to 10 grams in one day, which would reduce calories by 160. Stopped potato at lunch and added 1 glass of milk, with $\frac{5}{8}$ viij of cream, which gave a loss in calories of 75.

The progress of this case continued satisfactory. At one time

there was some difficulty in differentiating between the joint disease and the pain on motion from contracted tendons. Massage and passive motion were ordered to nearly all joints, and by June 28 she had almost full use of both arms and hands, and was prevented from walking only by the old contractures of her knees, which prevented their full extension, though they were responding slowly to passive motion. Baking of the knees was added about June 1 to precede the passive movements, in order to hasten the overcoming of the mechanical difficulties present.

July 1. Patient spent much time in a wheel-chair out of doors, and was about to return to her home. Her appetite, spirits, and color were excellent.

Diet consisted of:

Breakfast: Toast, 30 grams; butter, 3 grams; boiled rice, 25 grams (as a cereal); weak coffee, with 1 tablespoonful of cream and 1 teaspoonful of sugar.

Dinner: 1 chop, 70 grams (30 grams residue of bone), or 35 grams of chicken, beefsteak, or fish; butter, 3 grams; 1 glass of milk, with 2 tablespoonfuls of 20 per cent. cream; toast, 30 grams; raw tomatoes, 3 slices; weak tea, with 1 tablespoonful of cream and 1 teaspoonful of sugar.

Supper: Lettuce, with 1 tablespoonful of French dressing; toast, 15 grams; butter, 4 grams; milk (5vj), 1 glass, with 2 tablespoonfuls of 20 per cent cream; 1 egg (poached); raw tomatoes (2 slices).

July 4 she was up on her crutches twice a day and took a few steps without them. Could close her hands well and was everywhere free from pain unless tendons were put on the stretch. Could raise both arms high above her head and touch them. Said she was getting plenty to eat. Sent home with instructions. November 1, 1913. The patient was seen with Dr. J. E. Sweet and found not only to have maintained her improvement but to have made progress. She had adhered carefully to her diet and was free from active arthritis and pain.

CASE XIII.—Florence W., aged seventeen years, a well-built and well-nourished white girl; occupation, housework. Referred by Dr. Edward B. Hodge. Her previous history was free from evidences of tonsillitis, purulent infections, or other attacks of rheumatism. Ten months before admission, pain and swelling suddenly appeared in her hands, causing her fingers to flex sharply. Six weeks later the knees became affected, and then successively the feet, elbows, and shoulders, and on admission the jaws and cervical spine were also involved. Inquiry developed the fact that the girl had had a good appetite for her meals, but in addition had been exceptionally addicted to candy and cake, and confessed to having eaten before and during her illness whenever she could obtain any, which seemed to have been daily between 3 and 5 P.M.

On admission the patient was bedridden, and presented swollen, purplish fingers, the middle phalanges of which were very broad. The hands could not be flexed, and even passive motion excited great pain. The right elbow could be extended but slightly beyond 45 degrees, and the left not quite as much as 45 degrees, both being held in marked flexion. Motion in the shoulders was painful and limited; the cervical spine was somewhat involved; the jaws could not be opened wide enough for a satisfactory examination of her teeth; her knees were enlarged and bent to form angles of about 35 degrees.

X-ray examination of the abdomen showed no evident departure from the normal in regard to the position or shape of the stomach and colon. This was one of the few cases of which this was true. The hands showed active inflammation, with more or less absorption of the articular ends of the phalangeal bones. The metacarpals showed marked rarefaction of the distal ends and a fair amount at the proximal ends. The wrists were also markedly involved. The process as a whole was atrophic, the chief evidences of hypertrophy being in the shafts of the bones.

The urine was essentially normal and gave a negative indican reaction. Blood examination showed red blood cells, 3,830,000; white blood cells, 8300; hemoglobin, 56 per cent. Examination of the tonsils by Dr. N. P. Stauffer showed chronic tonsillitis. The ears were normal, but the teeth were in bad condition, showing discoloration and advanced decay, of the molars especially.

Upon admission to the ward on April 12, 1913, she was placed by the resident upon a semiliquid diet, pending further instructions. The intention had been to place her first upon a full house diet to determine approximately her normal intake, but inadvertently this was assumed to have been done, and for several days attention was focussed on certain experimental data in connection with the case, later to be referred to. Her weight on admission was 90 pounds and her diet averaged as follows. It was fairly generous, and yet much lower than the usual house diet, being semiliquid.

6 A.M.: Milk, f5 vj.

Breakfast: Toast, 28 grams, one good-sized slice; 1 egg, 50 grams; butter, 5 grams; milk (f5 vj), 1 glass.

Dinner: Toast, 26 grams; butter, 5 grams; strained vegetable soup, f5 vj; milk, f5 vj; egg-custard, 2 tablespoonfuls.

Supper: Toast, 30 grams; butter, 5 grams; hot milk, f5 vj; cold milk, f5 vj.

8 P.M.: Milk, f5 vj.

Frequently she did not take the second glass of milk at supper. When she took the whole diet as enumerated, however, she ingested approximately 1271 calories, which was a marked reduction from her previous intake, and, as just mentioned, was frequently further reduced. This yielded about 14 calories per pound of body weight or about 31 calories per kilo.

It should be noted that this case, like Case XI, was treated by dietary methods only, and in the face of an obvious source of infection in chronic tonsillitis and many carious teeth. She was ordered mouth washes because her breath was foul, and because this was the custom of the ward in all cases of pyorrhea and marked mouth neglect, but nothing was done in the way of extracting teeth or filling cavities and the like to achieve oral asepsis.

The ward notes recording the progress of the case follow:

April 26. (Abstract of several days.) Dusky purple color was much diminished in finger joints; the jaws had ceased to hurt. Knuckles were less painful and swollen.

April 30. Could flex and extend the knees considerably; the hands were nearly free from pain except on strong flexion by someone else, and motion was increasing daily. Both elbows were straightened to nearly the normal, and use of them was practically unrestricted.

May 8. Sitting in a chair every day. Fingers were changing shape as the swelling of the joints subsided. In common with some other cases in the ward she felt slightly stiffer, as the weather was fresh and cool.

May 17. Slept for the first time without a pillow under her knees to support them. Hands were doing exceptionally well, and she was able to squeeze an orange to obtain the juice. Muscles of arms and legs, were, however, much wasted.

June 5. Progress continued. Knees could be further straightened. Lateral pressure on the middle phalangeal joints caused pain only in the middle finger of the right hand. She practically had complete use of her hands.

June 28. The arthritis had subsided in the jaws, spine, shoulders, elbows, wrists, and fingers, but the difficulty of differentiating between the pain from contractures and that of joint disease *per se* made it difficult to tell whether the process was entirely quiescent in her knees. They were, however, becoming straighter, and for two weeks had received baking and passive motion frequently.

July 11. Improvement continued. November 3, 1913. Patient spent the summer at a seaside "home" where she adhered to her diet. In the fall she was sent to the Episcopal Hospital, Philadelphia, service of Dr. A. P. C. Ashhurst to have the old adhesions, etc., in her knees stretched or broken up. She was seen there with Dr. Hodge and Dr. Ashhurst on the above date and it was found that she had maintained her improvement. There was no active arthritis in any joint.

CASE XIV.—Miss W., aged twenty-one years; occupation, trained nurse. Her previous history was uneventful in relation to her present condition, and an examination revealed a well-built and fairly well-nourished girl who had complained for about a week of stiffness and pain in the hands and fingers upon waking

in the morning. She also felt drowsier than was proper, and found it difficult to begin the day's work. Her hands showed the profuse perspiration so frequently encountered in these cases, and distinct enlargement of nearly all the middle phalangeal joints of both hands. Either passive or active flexion of her fingers caused pain if attempted in the early morning, but later in the day this became less pronounced. By noon it was definite, though not great, in a few fingers only. Lateral pressure of the larger phalangeal joints elicited pain at any time. X-ray examination showed the stomach to be considerably enlarged and ptosed. The colon was exceedingly elongated and tortuous. The hands showed an inflammatory "fog" in the x-ray plate around nearly all the finger-joints, but the bones themselves showed little or no change. The soft tissue was swollen at all the middle phalangeal joints.

Close questioning revealed that the patient was in the habit of eating many sweets in addition to and between her regular meals, and that her appetite was excellent. Bowels were regular. Blood examination showed red blood cells, 3,110,000; white blood cells, 5020; hemoglobin, 60 per cent. Blood pressure was 129 systolic and 65 diastolic. Urine was normal, and a test for Indican was constantly negative. Her weight was 109½ pounds.

With the idea of determining what her average intake of food was, and therefore what it should be, a record was kept for nearly a week of all that she ate of the regular hospital training school diet. It averaged about 3004 calories, which yielded 27.3 calories per pound of body weight or 60 calories per kilo.

May 23, 1913. She was placed on the following dietary and instructed to avoid all sweets between meals.

Breakfast: 1 apple, 1 egg, 1 cup of coffee, weak, made with hot water, and f̄j of cream and 7 grams of sugar; 1 slice of toast and butter, 12 grams.

10 A.M.: 1 glass of milk, f̄j vj.

Lunch: Vegetable soup, f̄j viij; spinach, onions, lettuce, celery, asparagus, tomatoes, 2 tablespoonfuls of any two allowed, but no cream or thick dressing; oil and vinegar dressing for lettuce, f̄j j.

3 P.M.: 1 glass of milk.

Supper: 1 egg or a small slice of meat; green vegetables as at lunch; 1 slice of toast and stewed peaches; 1 glass of milk; 1 roasted potato; butter, 24 grams.

9 P.M.: 1 glass of milk.

This diet averaged in the neighborhood of 1900 calories or about 17 calories per pound of body weight or about 37 calories per kilo, a distinct reduction from that above cited.

In the fall of 1912 her weight was 120 pounds. When she began treatment it was about 110½ pounds, and on June 6 was about 109 pounds.

The notes of her progress follow:

May 25. Diet was begun May 23, at breakfast. Patient thought she felt brighter and more active in the morning. Bowels regular.

May 26. Awoke without any pain or stiffness in the fingers. Also felt brighter.

May 27. Fingers felt well, except for a slight sensation in the middle joint of the middle finger of the right hand. No pain anywhere else. She had a slight headache on waking. She was not unduly hungry.

May 29. Fingers were better even on pressure. Said she would adhere to this regimen because of the *bien aise*, even apart from the question of arthritis.

June 3. Doing well and improved steadily. Complained of nausea and a bad taste. Was given calomel and salts, as a result of which there was a slight loss of weight.

June 6. Fingers continued well, though there was a slight tenderness on forceful lateral pressure of two middle joints. Her menstrual period was about due, though she missed it the previous month. Felt lively and active.

June 25. Patient felt entirely well. Seldom thought of her hands, and only forcible pressure, as above, revealed anything abnormal. She thought this sensation was growing less, if anything. Because of her active duties in the ward the diet of this case was kept fairly liberal. Her weight was $107\frac{1}{2}$ pounds.

July 1. Weight, $107\frac{1}{2}$ pounds. Patient felt even better than on last note.

On December 1 she felt entirely well and was on active duty in the hospital wards.

CASE XV.—Miss P., a healthy looking girl, aged twenty years. Referred by Dr. Henry Pleasants, Jr., of West Chester, Pa. The patient was large, well-developed, of excellent color, and was inclined to be somewhat stout. The details of her previous history were kindly supplied by Dr. Pleasants: The girl had been healthy up to about twelve years, when she had an attack which the late Dr. John H. Musser thought suggestive of typhoid. She did not run a typhoid course, however, and returned home in a week or two apparently well, and had no further trouble of that nature. Later on, however, she had frequent attacks of tonsillitis. Six or eight years before she had scarlet fever, and a year or two later had measles. The rheumatic symptoms were more or less pronounced about that time. She had a distinct mitral murmur, and such marked joint symptoms that, five years before, her physician advocated having the throat attended to, and her tonsils were clipped by Dr. George Coates, with relief of the symptoms. In 1910 she had an attack of sinusitis, which seemed to precipitate all the old trouble, as she had been worse ever since. A year or so before, her physician noticed a marked atrophy of the muscles of the right hand with slight deformity, and consulted Dr. William

G. Spiller. He thought the condition one of rheumatic muscular atrophy. Previous to this, in the spring of 1911, there was noted a marked indicanuria and she was placed on colonic lavage. She also underwent a course of treatment at an orthopedic institute, and improved rather markedly under massage, baths, electricity, etc., but her symptoms would flare up as soon as she stopped treatment.

During the previous winter she developed slight tonsillitis again, and there was found a pus pocket in the left tonsil which it was thought might be responsible for some of her trouble. Dr. George Fetterolf was consulted, and agreed that the condition was pathological, but felt that there must be also some metabolic disturbance. She complained of so much pain in her foot that it was put in a plaster cast for two weeks, though without benefit.

On admission to the Presbyterian Hospital there was noted some questionable tenderness on deep palpation in the right iliac fossa. The heart was then without murmurs, the blood showed a trifling anemia, and the urine was normal to the usual tests, and at all times free from indican. She was generally constipated. The hands and feet showed, by the x-rays, widespread bone changes, but little involvement of the soft tissues. The thumbs were slightly subluxated on the carpi and the latter particularly showed both atrophy and hypertrophy, chiefly the former. The metatarsals of the feet were widely involved in the same way, and on the outside of the right foot near the phalangeal articulation was an erosion or hole large enough to admit the end of a pencil. (See Figs. and compare heels in plates of Case V). X-rays of the abdomen showed no great abnormality, though the splenic flexure of the colon was high and rather sharply bent. The blood pressure was normal. Her chief complaint was great tenderness under the ball of the right foot, preventing her rising on her toes or walking on the flat. Both wrists and some fingers of the left hand were sore, and had been so practically for years.

To ascertain her accustomed dietary, an accurate record was kept of all she ate, and its caloric value was approximated over a period of several days. It was found to be about 2500 calories or about 15.5 calories per pound or about 34 calories per kilo. This hardly equalled her usual intake, however, as she did not relish the hospital food, and ate less on that account, and, in addition, usually partook freely of sweets, ice-cream sodas, and candy especially.

May 26, 1913. She was placed upon a diet which, after some preliminary alterations and reductions, averaged as follows:

Breakfast: 1 apple, 135 grams; 1 egg, 54 grams; toast, 15 grams; butter, 10 grams; 1 cup of weak coffee, with 1 teaspoonful of sugar (f5j), and 2 tablespoonfuls of 20 per cent. cream, f5viii.

Dinner: Strained tomato soup, f5iv; spinach (about 100 grams)

or asparagus (109 grams), or one of the several other vegetables as mentioned in Cases XI, XIV, XVI, and others. One raw tomato; stewed fruit (without sugar), 63 grams.

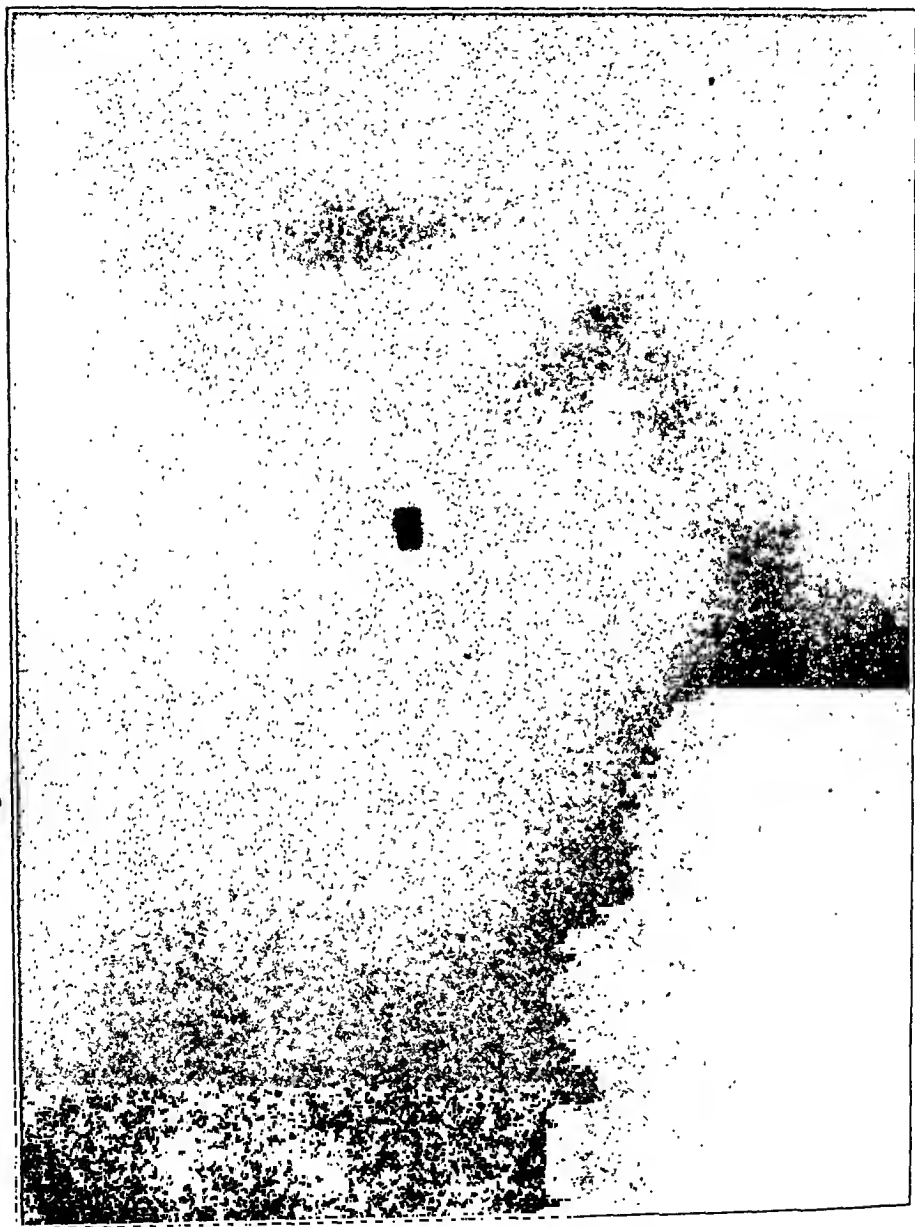


FIG. 1.—Case XV. Showing the apparent normality of bowel in an advanced case.

Supper: White meat of chicken or fish or chop or beefsteak, 125 grams; stewed figs, 2 tablespoonfuls (63 grams); weak tea, with $\frac{1}{3}$ iv of 20 per cent. cream (1 tablespoonful), and $\frac{3}{4}$ j (1 teaspoonful) of sugar.

Bedtime: 1 glass of milk, with 1 tablespoonful of 20 per cent. cream.

This yielded in the neighborhood of 1000 calories or about 6 calories per pound of body weight or 13 calories per kilo.

It should be noticed that as the body weight decreased on a fixed diet the calories per pound increased.



FIG. 2.—Feet of Case XV. Notice erosion at distal end of fifth metatarsal.

The condensed notes of her progress follow:

June 1. Foot hurt her considerably. There was a distinct diminution on pressure of the pain in the right wrist, which had been there, on pressure, since the summer of 1908.

June 7. Had been surprised to find that her right foot hurt less. She could stand relatively well on the toes of that side.

June 13. Pain in right wrist was certainly improved, and she could walk on the flat of her right foot fairly well.

June 18. The sore point on the ball of the right foot was better, but a new point of tenderness had arisen in the large toe-joint of the same side. This tenderness increased for several days, and then gradually subsided.



FIG. 3.—Feet of Case XV. Notice extensive erosion at the first metatarsophalangeal joint of right foot, the foot toward the left in the figure.

July 1. When she left the hospital she presented the following evidences of improvement: The pain under the ball of the foot was greatly diminished, so that she could walk with considerable comfort so far as it was concerned. The swelling and pain at the base of the big toe were much less, though still present after walking some little distance on it. The pain in the left wrist was entirely absent, and had remained so since its first disappearance. The

pain in her right wrist was difficult of location without considerable pressure and a search for it. One other old point of tenderness on her first left forefinger was better and another old point of tenderness on her left thumb was gone. Her weight was $147\frac{3}{4}$ pounds in her night dress. During the period of six weeks above described the patient spent every day in bed until 2 P.M., was restricted in her exercise, was given no medicine but cascara, and had lost 13 pounds in weight. She was far from well, but had made distinct progress, and was referred to her own physician for a continuance of the same regimen during the summer. A report on August 1 was of steady and continued improvement, with an increase in food and exercise, as per schedule. On October 7 she was practically free from pain everywhere, weighed $149\frac{3}{4}$ pounds in her clothes, could walk fast and well, and said she felt very much brighter and more active than before institution of treatment.

The analogy between the erosions in this patient's feet and those in the heels of Case V was interesting and close, making allowance for the greater duration of the disease in the present instance, Case XV.

CASE XVI.—Mrs. S., a well-built and well-nourished, active woman, aged fifty years. The patient had had no children, and gave a history of an attack of rheumatic fever at four years of age. Her health had otherwise been good until about twelve years previously, when she developed pelvic symptoms for which eight years before, both tubes and ovaries were removed. From this time her general health was again excellent. Her present trouble dated back seven years, when her knuckles began to grow stiff and slightly painful in the morning. This increased slowly and almost imperceptibly, until an exacerbation made her realize that the condition was progressing and limiting the use of her hands. In May, 1913, she experienced every morning on waking a stiffness and soreness in most of the larger knuckles of both hands, which made use of them painful and an effort. She ate generously, and was always constipated. Examination revealed a faint systolic mitral and a louder systolic aortic murmur. An x-ray examination of the abdomen revealed elongation and tortuosity of the colon, and of the hands showed soft tissue involvement, but little or no evidence of bony change. Her blood pressure and urine were normal, and she presented a slight secondary anemia. Her weight was 125 pounds. A record was kept of her food for about five days to determine her accustomed intake, and this was found to yield about 3000 to 3500 calories or nearly 24 calories per pound body weight or about 52 calories per kilo. She was then placed upon the following:

Breakfast: 1 apple, 1 egg, 1 slice of toast, 1 small piece of butter, 1 cup of weak coffee, with 1 tablespoonful of cream and 1 teaspoonful of sugar.

11 A.M.: 1 glass of milk.

Lunch: Vegetable soup, strained, f5 viij; any two of the following vegetables: spinach, raw or cooked tomatoes (without flour or cream gravies), turnips, onions (without thick dressing), squash, or cabbage. She was additionally allowed lettuce, with 1 tablespoonful of French dressing, and radishes.

4 P.M.: 1 glass of milk.

Dinner: Weak tea and 1 tablespoonful of cream and 1 teaspoonful of sugar; 1 average sized piece of butter; 1 moderate sized piece of meat of any kind; 1 roasted potato or an average helping of rice, spinach, or 1 other green vegetable (as lettuce); stewed fruit without sugar. This yielded about 1500 to 2000 calories or about 16 calories per pound body weight or 35 calories per kilo. She was also ordered to rest an hour in the morning and afternoon, as she was inclined to great activity, and was given cascara at night when necessary. The results were immediate and rather striking. She was started on the diet June 11 in the evening. On June 14 she felt well; a ring on one of her previously enlarged fingers came off most easily, and on waking on this date she felt no stiffness or pain in her hands or elsewhere. The patient was about to leave town for the summer, and an effort was made to increase her diet before she did so. The milk was given at meals instead of between, and she was allowed ice-cream at dinner. At the same time the weather grew warm and humid.

June 17. Patient weighed 125 pounds, and felt as well as on the date of the last note.

June 20. Patient felt a slight stiffness in the fingers; they were much better than before instituting treatment, but were not entirely supple on waking.

June 23. The fingers were almost the same as on the date of the last note, and she was returned to her first diet.

June 28. Fingers were improved.

July 1. The improvement was maintained or bettered and the patient left town.

July 10. The pain and stiffness were entirely absent, but the patient was somewhat under weight, as reported by letter.

CASE XVII.—J. C., aged about twenty-nine years, was in the service of Dr. Charles W. Burr, at the Orthopædic Hospital; and the writer is indebted for the privilege of including the case here. The patient presented the features of spondylitis rhizomélisque of the French, with great involvement of arms and legs and a "poker-back" spine. This case will later be reported in detail by Dr. Burr, and only an outline will be presented here. Unknown to the writer the general principles here described were instituted, about March, 1913, by Dr. Burr, who was familiar with some of the author's cases and treatment, and when the patient had shown clear evidences of improvement the writer saw him. Some few

changes were then made in the caloric intake, which was reduced to about 1546 calories, or at 103 pounds weight about 15 calories per pound or about 33 calories per kilo.

No obvious change took place in the man's spine, which was apparently ankylosed, but his arms and legs showed distinct improvement and progressed steadily. His hips and arms had been markedly involved on admission, but by July 10 he could walk and had good use of his arms and hands.

Many of the preceding cases had slight fever, but as they convalesced this grew less, and finally disappeared altogether on recovery.

METABOLIC AND OTHER OBSERVATIONS

CASE V.—Period 1. November 27 to December 5, 1912.

Metabolic observations conducted while the patient was actively ill.

	Nov. 27 Grams	Nov. 28 Grams	Nov. 29 Grams	Nov. 30 Grams	Dec. 1 Grams	Dec. 2 Grams	Dec. 3 Grams	Dec. 4 Grams	Dec. 5 Grams
Nitrogen of urine	8.6240	9.4080	8.9600	9.6320	9.5200	10.0840	
Ammonia of urine4080	.5168	.5984	.7072	.59845440	
Chlorides of urine	5.6000	8.4000	6.4000	7.6000	6.0000	6.0000	6.400	6.4000	
Titratable acidity of urine . .	1.6 OH	1.2160	.8960	1.1520	1.1520	1.1520	1.024	1.1520	$\frac{TS}{CS} = 11.4$
Δ of urine	—55°	—57°	—56°	—57°	—59°
Conjugate SO ₂ . .	.0821	.1064	.1806	.1477	.19301374	
Preformed SO ₂ . .	1.4175	1.4226	1.4054	1.5041	1.5330	1.5722	
Total SO ₂ . . .	1.4996	1.5290	1.5860	1.6518	1.7260	1.7096	

November 27. No indican. Patient has progressed favorably on metabolic diet.

December 2. For five days past has progressed steadily.

December 4. Pains and stiffness.

December 5. Felt well. Nitrogen of feces, 2.774 grams. Positive nitrogen balance of 1.67 grams. (The patient gained one-half pound during this five day period).

Period 2: February 7 and 8, 1913. Patient nearly well.

	Grams.	Grams.	
Conjugate SO ₂1425	.1797	
Preformed SO ₂	1.8900	1.6641	TS
Total SO ₂	2.0325	1.8438	CS = 12.

CASE VII.—Period 1: December 21 to 31, 1912. Ill health; though she felt some limited benefit from the metabolic diet,

	Dec. 21 Grams	Dec. 27 Grams	Dec. 28 Grams	Dec. 29 Grams	Dec. 30 Grams	Dec. 31 Grams	
Nitrogen of urine			7.840	7.9520	6.4960	6.4960	
Ammonia of urine5984	.5440	.4896	
Chlorides of urine				4.0000	4.0000	4.4000	
Titrate acidity of urine	Na .3618 OH		Na 1.024 OH	.8960	.8960	.8960	
Δ of urine				— .62°	— .57°	— .56°	$\frac{TS}{CS} = 9.1$
Conjugate SO ₃1100	.1172	.1604	.1275	.1412	
Preformed SO ₃		1.1303	1.0790	1.0907	1.0289	.9714	
Total SO ₃		1.2403	1.1962	1.2511	1.1564	1.1126	

December 28, felt surprisingly well.

December 29, was still fairly well.

December 30, was not so well.

December 31, had pains and stiffness.

Period 2: February 1 to 3, 1913. Convalescence.

	Feb. 1. Grams.	Feb. 2. Grams.	Feb. 3. Grams.	
Nitrogen of urine	6.9614	6.9140	6.4060	
Ammonia of urine3212	.2720	.1904	
Chlorides of urine	6.6165	5.2000	4.8000	
Titrate acidity of urine6420	.6100	.7040	
Δ of urine	— .83°	— .79°	— .75°	
Conjugate SO ₃1124	.1015	.1056	$\frac{TS}{CS} = 9.9$
Preformed SO ₃9535	.9809	.9136	
Total SO ₃	1.0659	1.0824	1.0192	

CASE VIII.—Period 1: February 8 and 9, 1913. Ill health.

	Grams.	Grams.	
Conjugate SO ₃1078	.0885	
Preformed SO ₃	1.5718	1.4787	
Total SO ₃	1.6796	1.5672	
TS		15.5800	17.5900
CS			

Period 2: April 11 and 12, 1913. Convalescence.

	Grams.	Grams.	
Conjugate SO ₃1337	.1598	
Preformed SO ₃	1.6389	1.4038	
Total SO ₃	1.7726	1.5636	
TS		13.2000	9.7800
CS			

The ethereal sulphates were both relatively and actually higher during the period of convalescence. The ratio of $\frac{TS}{CS}$ was high in Period 1.

1 When on house diet.

A consideration of the metabolism as evidenced by these figures corroborated the figures and views advanced in the preliminary report, based on Case II and Case III. The methods employed were the Kjeldahl for nitrogen; Folin's method for ammonia; the Volhard-Arnold method for chlorides; Folin's method of precipitation with potassium oxalate for acidity, the Beckmann-Heidenhain apparatus for Δ , and Folin's method for the sulphates and creatinin.

The nitrogen and ammonia showed nothing which could not be encountered in health.

The creatinin as studied in Cases II (J. H.) and Case III (Mrs. F.), was about normal, and suggested no disturbance of the internal muscular metabolism as far as the creatinin output could be regarded as an index of this.

Turning to the titratable acidity of the urine, it appeared that the evidence here was also within the limits of health, and that distinct variations clinically in the condition of the patient were not always reflected in the urinary acidity. At least there was no ground for more definite conclusions on that score. Observations are pending on the *true* acidity or hydrogen ion concentration of the urine.

In an attempt to observe some of the more imponderable elements of elimination, estimations were made of the depression of the freezing-point (Δ) as an evidence of the molecular concentration of the urine. Observations were also included on the chlorides as a partial control of this. Any marked variation of Δ can in most cases be traced to a disordered kidney function if the influence of such factors as the chlorides be appreciated. The results were negative, however, and what has been said of the titratable acidity also applies here. These negative results, however, were in consonance with those of the estimation of urea and non-coagulable nitrogen of the blood, and also with those of the phenol-sulphophthalein test of kidney function, later to be described.

On the basis of this agreement it seems clear that the disease under discussion is not referable to faulty elimination in the usual sense of the word.

The ethereal sulphates were formerly regarded as a dependable criterion of so-called intestinal putrefaction, but some recent work by Folin has cast doubt upon this, and the question is somewhat *sub judice*. Indican is now regarded as reliable evidence of putrefaction, however, by most authorities.

It was pointed out previously² by the writer that if the conjugate or ethereal sulphates be an index of so-called intestinal putrefaction this last condition is not a factor causative of rheumatoid arthritis. Further observations, as the appended tables show, entirely support this view, and, further, are themselves additionally corroborated by later clinical evidence.

² AM. JOUR. MED. SCI., October, 1912.

The actual and relative outputs of the ethereal sulphates, as compared with the total sulphates, show either no important variations in the periods of ill health and disease or else show an actual and relative increase during convalescence.

The metabolic figures of Case II (*loc. cit.*) were given for what they were worth, but since no control observations could be made during marked improvement their value is minimized. They show nothing that could not be encountered in health, though the ethereal sulphates were conspicuously low as compared with the next case, and, indeed, are low for any individual who suffers much from constipation.

Turning to Case III (*loc. cit.*) and comparing the ethereal sulphates of Period 1 with those of Period 2, there was found in the latter, when the patient was improving rapidly, a surprising rise associated with a decrease or absence of indican. Whereas they had averaged in Period 1 about 0.3805, they rose in Period 2 to 0.4457, an increase of 17 per cent. The ratio of conjugate to preformed sulphates in the first period was 1 to 6.4; in the latter period it rose to 1 to 4.3 in spite of ample daily bowel movements and lavage of the colon.

In Case V, there was no important change in the averages of the two periods, though the ethereal sulphates rose steadily during the improvement of Period 1 and dropped on a "bad" day.

In Case VII there was no great difference in the averages of the two periods, but in Case VIII the relative and actual values of the ethereal sulphates rose conspicuously during convalescence.

Continued and repeated observations were made for the presence of indican in all these cases, but it was rarely present during either ill health or convalescence, and in no case was it present more than exceptionally and at considerable intervals. As detected by Obermayer's reagent, it can be said to be an infrequent accompaniment of the urine in rheumatoid arthritis, and seems to bear no relation to it. Whichever of these criteria be accepted as to the existence of intestinal putrefaction the evidence is the same.

During the first metabolism period of Case VII, it was noted that, as with Case III and Case V, the reduced intake of food incidental to the monotony and simplicity of a metabolic diet was of unintended benefit, so that all three patients experienced a distinct but limited improvement. In Case VII this was apparent on December 28, when she had had no real bowel movement for four days.

Constipation certainly constitutes a most important factor in intestinal putrefaction, but in spite of it then and later, she showed improvement.

By the same token, colonic lavage had been used by the writer and regarded as useful in Cases I, II, III, IV, and VI but on the strength of the observations above noted it was dispensed with

in Case V, and in all but the next two, subsequently, with entire success.

Analogously the influence of the fecal bacteria, which was thought to be a possible factor in the earlier cases and led to the administration of buttermilk, was made to seem less important by the observations on the sulphates. This led to the substitution of whole fresh milk and other food in Cases V, VI, and others, with even better results. Again, the changes of diet in Case XI and Case XII from relatively high carbohydrate to relatively high proteid, of equal caloric value, showed conclusively, if further proof were needed, that the proteids could not be regarded as the harmful agents, except in the sense of metabolic limitation for both carbohydrate and proteid, as elsewhere noted.

The futility is apparent of observing the "no red-meat" dictum, long advocated in the treatment of this condition, by most clinicians, and even yet obtaining with many.

In point of fact, many of the cases here cited were given eventually meat of all kinds as their largest source of proteid. It may be mentioned that another popular fetish of "acids and fruits" also finds no support in the above data, and in fact tomatoes, apples, and vinegar in salad dressing have been used with greater freedom than most articles in supplying harmless but satisfying food to this series of cases.

(To be continued.)

REVIEWS

A PRACTICAL TREATISE ON MEDICAL DIAGNOSIS FOR STUDENTS AND PHYSICIANS. By JOHN H. MUSSER, M.D., LL.D. Late Professor of Clinical Medicine in the University of Pennsylvania, etc. Revised by JOHN H. MUSSER, JR., B.S., M.D. Instructor in Medicine in the University of Pennsylvania; Physician to the Philadelphia Hospital; Assistant Physician and Physician to the Medical Dispensary of the Presbyterian Hospital, etc. Sixth Edition; pp. 793; 196 illustrations and 29 colored plates. Philadelphia and New York: Lea & Febiger, 1913.

DURING the decade that has elapsed since the fifth edition of Musser's *Medical Diagnosis* appeared, great changes have been wrought and far-reaching advances have been made in the study of medicine. It is not surprising, therefore, that during the last few years this now famous work should have lost some of its former usefulness. Revision was urgently needed. The medical profession will, therefore, welcome with enthusiasm the recent new sixth edition of this foremost American work on medical diagnosis, which now has been virtually rewritten and brought thoroughly up to date by the energetic and well-directed efforts of Dr. John H. Musser, Jr.

During the course of five editions the older work had attained the unwieldy size of 1213 pages; the new book has been wisely reduced to 793 pages. This reduction in size has been accomplished by eliminating certain sections that were out of date and by the careful condensation of others. The new edition follows the older one in its general arrangement and covers the subjects with equal thoroughness, but more concisely. For example, where in the fifth edition four chapters were devoted to a discussion of the clinical history, in the present edition that subject is adequately disposed of in a single chapter.

It would be impossible to discuss in detail the numerous improvements or to enumerate the many minor alterations that are to be noted in the new work. It is sufficient to call attention to the most noteworthy features of this edition. The chapter on cardiovascular diseases has been carefully rewritten and in its present form embodies the most approved teachings on this subject. The subject of blood pressure is well considered, and the auscultatory method for its determination advocated. The modern conception of arrhy-

thymia is set forth; the ink polygraph of Mackenzie is described, as are various pulse tracings and the method of their analysis. The electrocardiograph and electrocardiograms are described and illustrated and the interpretation of the latter is discussed.

The section on laboratory diagnosis shows careful revision. Nearly all the routine laboratory methods that have proved of value are detailed. It might have been well to have included the polaroscope under the various tests for glycosuria. The Wasserman reaction and Noguchi's modification of this test, as well as the latter's butyric acid test, are clearly detailed. An entire chapter is devoted to emphasizing the functional tests of organic efficiency that are daily becoming more important, as, for example, the phenolphthalein test for renal sufficiency, Strauss' test in hepatic conditions, and the most useful of the pancreatic tests.

The chapter on specific infectious diseases have been altered so as to conform to the many recent modifications that have taken place in our conception of these conditions, and an entirely new chapter has been added on diseases due to animal parasites.

The earlier editions were noteworthy because they contained such a fund of valuable observations and suggestions, based upon the enormous clinical experience of their author. In the new edition these products of a ripe experience have not only been skilfully preserved, but amplified by the addition of the best and newest advances in medical diagnosis. The author of this revised edition is to be congratulated upon having performed so thoroughly and satisfactorily a difficult task. A comparison of the new Musser's *Diagnosis*, with other works of similar scope, leads one to the conviction that in its present form it represents the most convenient, complete, concise, and practical book on medical diagnosis that is available for students in this country. As a consequence, it has already received, and should continue to be accorded, a widespread and hearty reception from the medical profession of America.

G. M. P.

THE SURGERY OF ORAL DISEASES AND MALFORMATIONS: THEIR DIAGNOSIS AND TREATMENT. By GEORGE V. I. BROWN, D.D.S., M.D., Oral Surgeon to St. Mary's Hospital and to the Children's Free Hospital, Milwaukee; Professor of Oral Surgery, Southern Dental College, Atlanta, Ga. Pp. 740, with 359 engravings and 21 plates. Philadelphia and New York: Lea & Febiger.

THE title of the book is somewhat misleading in that it deals with a number of subjects that have only an indirect relation to the surgery of the mouth. For example, Chapter V, comprising

some 150 pages, is devoted to the diseases of the nervous system, including a great variety of lesions of the spinal cord, brain, and cranial nerves—*anterior poliomyelitis*, *amyotrophic atrophic sclerosis*, *cerebral hemorrhage*, *embolism and thrombosis*, *facial paralysis*, *tinnitus aurium*, etc. The subjects are presented in a concise and interesting way, but many of them are well without the scope of the oral surgeon. The volume comprises a great deal of the subject matter one would expect to find in a regional surgery of the head and face, including, of course, the buccal cavity, and should, therefore, be of interest not only to the dental surgeon, but to the general surgeon as well. The chapters in which the author has left his personal impress most strongly are well within the special field of oral surgery. These are devoted to harelip, cleft palate, and defects of speech, to nasal deformities and diseases in relation to the maxillæ, and diseases, injuries, and malformations of the lip. Although these are treated in but three of the thirteen chapters, they contain a vast amount of interesting material and enough to justify the purchase of the book for any one interested in these problems. Dr. Brown has an unusually broad vision of the possibilities of the oral surgeon, and this together with his unusually large experience makes him peculiarly justified to discuss the problems in an authoritative way. He has been particularly happy in the selection of his illustrations, and describes with unusual clearness of expression the various operative procedures, many of them of his own devise. C. H. F.

MASSAGE: ITS PRINCIPLES AND TECHNIQUE. By MAX BÖHM, M.D., of Berlin, Germany. Edited, with an introduction, by CHARLES F. PAINTER, M.D., Professor of Orthopedic Surgery at Tufts Medical School, Boston. Pp. 91; 97 illustrations. Philadelphia and London: W. B. Saunders & Co., 1913.

THE American editor of this treatise states that in Germany physical therapeutics in all its forms is employed more widely than it is here and he deplores the lack of knowledge of the benefit to be derived from proper massage: Hence this translation. In the author's introduction it is stated that the work is written as a compromise in the question, "Who shall give massage, Doctor or Layman?"

The author states that back massage, common flat-foot, abdominal massage and general massage may with confidence be given to assistants. But for pathologic changes in the muscles, tendons, joints, nerves, internal organs and abdominal adhesions, the eye, the larynx, etc., treatment by a trained specialist is much to be

preferred. The technique is essentially that employed in Hoffa's clinic and it is unexcelled for orthopedic work.

Anatomy is mostly omitted and very properly.

One impression is obtained that justifies criticism: We refer to the ending of the translation. Some sentences do not read smoothly and at times the meaning is not at once clear. A case in point is under the heading of Massage of the Nerves and Skin, on page 78: It reads, "How much prospect of curing or mitigating paralysis is offered by massage, when it is indicated, and when useless, this decision, of course, requires an exact knowledge of the disease in question."

The illustrations are admirable and convey the idea of the work as clearly as it is possible for pictures to do. There is a great deal about massage that is not found in this book but, strictly speaking, such matter does not belong to orthopedic work. N. S. Y.

THE PRACTITIONER'S VISITING LIST. "Weekly," dated for 30 patients; 32 pages of data and 160 pages of classified blanks. Philadelphia and New York: Lea & Febiger, 1914.

THE widespread use of this *Visiting List* year after year eloquently attests its value to the medical profession. It is arranged in various styles, so as to meet the requirements of every practitioner. Moreover, it contains much information of a practical sort that is of the utmost value to the busy physician. Experience has shown that this *Visiting List* is a decided aid to the efficient and accurate conduct of a medical practice. G. M. P.

MEDICAL AND SURGICAL REPORTS OF THE EPISCOPAL HOSPITAL.
Vol. I, pp. 402. Philadelphia: W. J. Dornan, 1913.

THESE reports from the Episcopal Hospital staff are preceded by a short historical sketch of the institution and the report of the Superintendent for the year 1912. Following this there are a series of papers, edited by Ashhurst, representing the original work and investigations of the various members of the Staff, as well as reports of the interesting and instructive cases that have occurred in the wards or in the dispensaries. Much of this material has been published elsewhere, though a few of the reports make their first appearance in the present volume.

The papers are for the most part well worth reading, and are deserving of commendation. Particularly meritorious are the fol-

lowing: the contributions of Ashhurst, who presents a series of papers upon bone surgery and a comprehensive article upon the treatment of tetanus; a paper by Piersol dealing with the significance and management of extreme hypertension; a report by Stevens upon malignant disease of the lung, and a brief sketch by Eves of some overlooked causes of cough. J. H. M., JR.

BEITRÄGE ZUR KLINIK DER INFEKTIONSKRANKHEITEN UND ZUR IMMUNITÄTSFORSCHUNG. Edited by PROFESSOR L. BRAUER, Medical Director of the General Hospital of Hamburg, Eppendorf. Volume I, No. 1, Pp. 227; 5 Tables (2 in color), 10 Stereoscopic pictures and 5 text illustrations. Würzburg: Curt Kabitzsch, 1912.

THIS journal is the third of a series of "Clinical Contributions" by the publisher; the others being, "Contributions to the Clinic of Tuberculosis" and "Journal for Tuberculosis Research." Judged from the appearance of the first issue of the publication, it promises to be exceedingly well edited, comprising in the list of collaborators many of the leading medical scientists of Europe engaged in research on infections and immunity. The reputation and character of the work of the publisher is such as to guarantee the production of excellent illustrations. The content of the first issue is in part as follows: Euerasia and Anaphylaxis; The Prevention of Transmission of Acute Infectious Diseases in Hospitals; Concerning the Duration of Passive Immunity; The Etiology of Puerperal Infection.

Obviously, the pertinence of these topics, presented by recognized authorities, to current medical literature is not only indisputable, but of such interest and importance as to make their perusal obligatory to anyone professing modern ideas and familiarity with the subjects of infection and immunity. B. A. T.

GENERAL PARESIS. By PROFESSOR EMIL KRAEPELIN. Authorized Translation by J. W. MOORE, M.D. Pp. 200; 48 illustrations. New York: Nervous and Mental Disease Publishing Co. 1913.

THIS is a translation of the chapter on paresis from Kraepelin's text-book on psychiatry. Heretofore only the "Introduction to Clinical Psychiatry" has been available in English. It is an excellent exposition of the clinical signs of paresis and would be of the postmortem findings, were it not for the fact that within a few months the spirochæte has been found in the brain of paretics and as a consequence its entire pathology will have to be rewritten. T. H. W.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Cultural Results in Hodgkin's Disease.—BUNTING and YATES (*Arch. Int. Med.*, 1913, xii, 236) have secured a pure culture of a pleomorphic diphtheroid organism in 3 cases of Hodgkin's disease. In two other cultural attempts the organism was recognized, but was not secured in pure culture, and in a sixth case a similar organism, morphologically, was stained in the lesions of a primary intestinal Hodgkin's case. The organisms grow luxuriantly on glycerin-phosphate-agar under both anaërobic and aërobic conditions. Long, granular, banded, and club-shaped involution forms appear on dry medium. On moist serum the organisms are short and plump, with polar staining. Many of these forms are coccoid. The organism stains by the Gram method. It is not acid-fast. Bunting and Yates feel they are dealing with the same organism described by Negri and Mieremet, and the latter's results, combined with the authors', indicate strongly they are dealing with the cause of Hodgkin's disease. The morphological elements obtained by Fränkel and Muck, by the antiformin method, in 12 out of 13 cases are so similar as to be added support. Animal experimentation is in progress. The name suggested for the organism is *Corynebacterium Hodgkini*. The frequent finding of a white staphylococcus, plus the polymorphonuclear leukocytosis, occurring late in the disease, suggest that possibly a secondary infection plays a part in the development of the disease.

Inequality of the Radial Pulses in Chronic Syphilitic Aortitis.—LAIGNEL-LAVASTINE and VINHIT (*La Presse Med.*, 1913, p. 607) have observed unequal radial pulses in three patients in whom radioscopy determined the absence of an aneurysm. In all, the left was smaller

and delayed as compared to the right. All the patients had syphilis. Two had aortic insufficiency. In each the aorta was elongated, a little dilated and tortuous, but no trace of an aneurysm was demonstrable. This was confirmed at autopsy in one case. It is striking that the inequality was much less marked in one case after mercurial treatment.

Pulsus Alternans in Myocardial and Arterial Disease.—With a view to ascertaining the value of pulsus alternans as a sign of disease of the heart, its frequency in different conditions, and its prognostic significance, WINDLE (*Quart. Jour. Med.*, 1913, vi, 453) has analyzed 33 cases coming under his observation. In order of frequency it occurred in the following conditions: (1) Arterial and myocardial disease; (2) chronic heart disease due to rheumatism; (3) pneumonia; (4) paroxysmal tachycardia; (5) acute rheumatic carditis. Ten cases were still under observation, but in more or less serious condition. Fourteen cases were fatal. Pulsus alternans was present in each patient when coming under observation. One case lived nearly two years. The rest died within a year. Nine other fatal cases developed pulsus alternans while under observation. The time of inception was known within a year; 2 lived eighteen months, and 2 twenty-four months. This supports Mackenzie's experience that the inception of pulsus alternans in aged people has invariably been followed by fatal heart failure within two or three years. In the 9 cases, last mentioned, there was no evidence of disease on clinical examination, except the pulsus alternans, to warrant a grave view being taken of the prognosis. When once present, pulsus alternans will never again be absent for long, because the exhaustion of the heart which it expresses is due to degeneration of the heart muscle. In the early stages alternation becomes latent for a time through bodily rest, or the action of drugs which slow the heart, but it eventually persists with rest and in spite of any measures of treatment yet tried.

Diagnosis of Typhoid Fever on Admission to a Hospital.—SHATTUCK and LAWRENCE (*Boston Med. and Surg. Jour.*, 1913, clxix, 228) believe typhoid fever should be suspected in patients entering a hospital after suffering from febrile conditions of a few days' duration. They should be treated under precautions to prevent the possible spread of infection. In a series of 100 non-typhoid patients of fourteen years of age or older, in which typhoid fever was suspected, bronchitis, bronchopneumonia, and influenza represent 29 per cent., or nearly one-third of the whole, undiagnosed fevers 15 per cent., gastro-enteritis, diarrhea and colitis, 12 per cent. They emphasize the importance of the differential diagnosis. The absence of rose spots at first examination has the same little weight for diagnosis as splenic enlargement not demonstrable by palpation and a negative Widal test. The absence of leukocytosis in a febrile disease strongly suggests typhoid fever. A count below 5000 is unusual in conditions simulating typhoid. A white count above 9000 is presumptive evidence against typhoid. Ordinary bronchitis, as a rule, entered the hospital during the first week, and typhoid with signs of bronchitis generally during the second week of illness. Congestion of the bases of the lungs, when present

in febrile disease, uncomplicated by cardiac insufficiency, points to typhoid. The high temperature; seldom below 101° , and the low pulse rate are also helpful.

On Negative Pressure in the Marrow of the Long Bones of the Dog.—E. O. P. SCHULTZE and P. J. BEHAN (*Münch. med. Woch.*, 1913, lix, 2849) make a preliminary report on observations they have carried on, on pressure in the marrow of the long bones. They had expected to find a pressure corresponding about to that in the capillaries which Landois gives as 18 mm. Hg. To their surprise, they discovered a negative pressure which equaled 18 to 22 mm. of normal salt solution. Numerous experiments verified this finding. They believe a negative pressure is due to the suction of the veins, whose stomas are found in the marrow. To prove this the venous circulation was interrupted with a bandage, and the negative pressure disappeared.

The Occurrence of Ferments in the Cerebrospinal Fluid in Various Psychic Disorders.—SZABÓ (*Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1913, xvii, 145) investigated the ferment action of the spinal fluid in 60 cases, of which 27 were general progressive paralysis, 5 epileptics and alcoholic psychoses, the remainder being cases of hysteria, senile dementia and manic-depressive insanity. Fluid, withdrawn before the noon-day meal, was not centrifuged. Occult blood was ruled out by the benzidin test. Diastase was determined by Wohlgemuth's method—invertase by the polarimeter, pepsin by the ruin and cdestin tests. The presence of trypsin, lipase oxydase, lactose, and other ferments was tested for by customary methods. The results were similar to those of Kafka; normal fluid contains few, weakly acting enzymes; diastase occurs mainly in dementia præcox, alcoholic psychoses, senile dementia. Lipase can be detected in normal liquor, but is especially potent in cases of general paresis. Szabó thinks the ferments arise from disintegrating cells and from the secretory activities of the choroid plexus.

On the Crescendo Murmur of Mitral Stenosis.—D. GERHARDT (*Münch. med. Woch.*, 1913, lix, 2713) reports observations on the crescendo murmur of mitral stenosis which militate against the view expressed by Brockbank in 1909 to the effect that this murmur is due to the passage of blood from ventricle to auricle. In other words, Gerhardt does not agree with Brockbank that the murmur is one of insufficiency of the mitral valves. Brockbank argues that the thickened stiff valves do not close as they normally do at the beginning of the ventricular contraction but only after the systole has reached a certain degree of intensity. The murmur produced by the flow of blood backward into the auricle increases in intensity with the increasing force of ventricular contraction ceasing with the first sound. In some cases of mitral stenosis, Gerhardt points out the presystolic murmur is separated from the first sound by a definite pause; in these cases the crescendo quality of the murmur is largely lacking and the snapping character of the first sound is not heard. In numerous cases of mitral stenosis with partial or complete block, one can often hear the gradual loss of the crescendo quality of the murmur, especially

when there is a progressive increase in the interval between the contraction of auricle and ventricle, until, perhaps, after five or six beats the ventricular contraction fails, and the cycle starts again. With the first three or four beats of such a cycle a presystolic murmur ending in a snapping first sound is heard; then a definite interval between murmur and first sound occurs, and with it the crescendo quality is lost. During the ventricular intermittence one also hears a simple short murmur. Occasionally in cases of stenosis with perpetual arrhythmia one hears diastolic murmurs with crescendo character, though in the majority of cases of perpetual arrhythmia the murmur disappears. With the reestablishment of normal rhythm, as may occasionally occur, the murmur returns. The fact that the auricle is fibrillating when perpetual arrhythmia is found, together with the fact that the murmur is lost, points strongly to the auricular origin of the murmur. In certain cases of mitral stenosis with perpetual arrhythmia, Mackenzie has observed that the typical crescendo murmur ending in a low first sound may at times be heard. If one auscults such cases when the rhythm is slow, it is seen that the murmur becomes protodiastolic and decrescendo, and is separated by a definite interval from the first sound. With an increase in frequency of the rhythm, the crescendo murmur ending in a snapping first sound returns. Gerhardt concludes, therefore, that a diastolic mitral murmur, whether due to protodiastolic filling of the ventricle or to contraction of the auricle, takes on a crescendo quality with a snapping first sound, wherever the murmur is interrupted by ventricular contraction. The crescendo quality is lost when the murmur and first sound are separated by a definite interval. In all cases where the pulse is regular, Gerhardt believes the murmur is due to contraction of the auricle.

A New Theory of Graves' Disease.—In certain districts along the coasts of Spain it is not uncommon to see individuals who present a combination of myxedema and Graves' disease. MARIMON (*Berl. klin. Woch.*, 1913, I, 1296) cites this as further evidence against the time-worn theory of dysthyroidism advanced to explain the symptoms of exophthalmic goitre. The theory is put forward that Basedow's disease is really due to an insufficiency in thyroid secretion. For some reason, the gland becomes unable to metabolize all the iodine which is brought to it: this iodine excess in the circulating blood, as Klose, Lampé, and others have shown, influence both the vagus and sympathetic nervous systems, and preëminently the nerve mechanisms of the heart. Myxedema and Graves' disease are two different syndromes, expressions, however, of one and the same pathological process. The former is due to a lack of sufficient metabolized iodine, whereas the latter is the result of the action of excessive unmetabolized iodine. In support of the theory Marimon gives the results of experiments conducted upon thyroidectomized dogs. When the juice of pigs' thyroids was injected in such animals intravenously, there resulted tachycardia and in one instance, pronounced exophthalmos. Marimon interprets this by assuming that the iodine in the thyroid juice, plus that taken in with the food was not metabolized by the dogs, and hence the symptoms of Graves' disease resulted.

SURGERY

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Resection of the Stomach and Colon for Certain Forms of Gastric Carcinoma.—PERTHES (*Zentralbl. f. Chir.*, 1913, xl, 1097) says that surgeons are divided on the question of what to do in cases of gastric carcinoma with adhesions to the meso-colon, the excision threatening gangrene of the transverse colon. Some surgeons regard these cases as inoperable, while others do not. Some will first resect the carcinomatous portion of the stomach and then decide whether or not the colon should be resected for threatened gangrene. Perthes advises in all cases in which the branches of the colica media are involved in the carcinomatous process, that the operation from the beginning should contemplate a simultaneous resection of the transverse colon, great omentum, meso-colon and stomach. When the abdomen is opened and a gastric carcinoma is found, which is removable, but adherent to the meso-colon, an opening is made in the meso-colon and the relations of the cancer to the pancreas determined. Firm adhesions to the pancreas will decide that the cancer is inoperable. If such adhesions are not present and the branches of the colica media are involved in the carcinoma, the meso-colon is ligated and divided centrally from the growth, and the transverse colon is clamped on both sides of the division of the meso-colon, and divided between the clamps. The two divided end are immediately closed. Then the gastro-hepatic omentum is ligated and divided along the lesser curvature, and the duodenum divided between clamps and closed as in the Billroth II resection of the stomach. The meso-colon, transverse colon and stomach are then divided on the oral side, in a similar manner and the whole diseased tissue removed in one piece. This gives a good exposure of the region behind the stomach, for finding and removing involved lymph glands. The whole transverse opening of the gastric stump is anastomosed to the uppermost loop of the jejunum. The closed stumps of the colon are then anastomosed, side to side. Sometimes it will be necessary to mobilize the hepatic and splenic flexures of the colon in order to bring the two stumps together properly. Perthes has done this operation in 4 cases. One patient died 5 days after operation from pneumonia. The 3 other patients were discharged healed. This mortality is just the same as for resection of the stomach for carcinoma, in general, in the Tübingen clinic, in the last two and a

half years. Two of the patients upon whom the gastrocolic resection was performed, were doing well and gaining weight, seven and six months after operation. A markedly emaciated woman operated on four months before, presented herself recently in very good condition, free of all stomach trouble, but there was a suspicious tumor in the abdominal wall.

Posterior Drainage of the Pericardium and Pleura.—TIEGEL (*Zentralbl. f. Chir.*, 1913, xl, 900) says that operations on the heart are usually so pressing that the asepsis, both in the preparation and during the operation, is too hurriedly carried out. In two operations which he performed, with the patients almost *in extremis*, the question of effective drainage of the pericardium and pleura came up, as infection of both cavities was expected. Statistics show a high percentage of operative infections. Grassman, in 1908, from a statistical study, found that 42 per cent. of operations on the heart were fatal from infection, and of those which were followed by recovery, in 60 per cent. the healing was complicated by infection. Hesse from the same kind of study, found similar results. They speak strongly against primary closure of the wound, especially when asepsis cannot be provided. Tiegel thinks that the drainage should be dependent, if possible. He has convinced himself from cadaver studies that this does not offer particular technical difficulties. It will be desirable only when there is a large simultaneous opening of the pleural cavity, which is the rule in heart operations. The external opening of the drainage tube must be provided with an exact valve, such as is now used for pleural drainage. After the conclusion of the operation on the heart and suture of the pericardial opening, the lung, somewhat above and laterally, is pushed aside and a low forceps is pushed backward, between the lung and pericardium to one of the posterior intercostal spaces, opposite the anterior wound. This is accomplished very easily. The patient is then turned on his right side and where the skin is made prominent posteriorly by the forceps, the skin is painted by tincture of iodine and is incised to the point of the forceps which is then pushed through this small wound. By means of a probe, the desired length of the drainage tube is measured, so that the valve at its outer end will fit properly over the posterior opening in the chest wall. The tube is introduced through this opening and the pleural cavity and a small opening, made in the posterior wall of the pericardial sac, to which it is sutured. The operative wound anteriorly is then closed and the dressings applied.

Lengthening Shortened Bones of the Leg by Operation.—MAGNUSON (*Surg. Gynec. and Obst.*, 1913, xvii, 63) determined by experimental work on the lower animals that long bones could be lengthened, and in one patient demonstrated the practical value of his deductions in the human. He says that a shortened femur may be lengthened from two to three inches without any interference with blood and nerve supply, excepting in cases where there is a large amount of old inflammatory tissue which would limit the stretching of the bloodvessels and nerves, or which might produce kinking. Ivory, being an animal matter, is entirely absorbed by the tissues, does not act as a foreign

body in bone, does not cause necrosis or slough out as do most other materials. Ivory screws may be cut off flush with the shaft of the bone, leaving nothing to project into or irritate the soft parts. There is no flange or shoulder on the screw to prevent it from entering to its full length. The method of application insures the screw fitting accurately into the hole made for it, since a tap is put through first; the deep thread into the bone insures a good hold, prevents any lateral motion, and the absorption of fluids by the ivory insures that in twenty-four hours the screws will fit so closely that it will not allow the slightest motion between the fragments. No great force is needed to drive the screws in, and eventually they will be absorbed, leaving the healed bone without defect. In cases of infection after the operation the ivory will not be absorbed until the suppuration has ceased. Lengthening bones would be of benefit in shortening after fracture, faulty development, or injury to the epiphysis before full growth is reached. The amount of extension obtained in these experiments was from three-eighths to one-half inch in dogs, about the size of a fox terrier without the slightest injury to bloodvessels or nerves, making it seem very probable that from two to three inches may be obtained in a bone as long as the average human femur, without serious after effects. The method of sterilization of the ivory screws found best, is saturated solution of bichloride of mercury in alcohol, placed in the autoclave, under high steam pressure, for four hours. If these ivory screws are boiled they become warped and useless.

The Pathogenesis of Prostatism.—DETON (*Jour. d'Urolog.*, 1913, iv, 233) with Caspar, studied the bladder in the cadavers of old people with relation to the problem of prostatism. The histological examinations emphasized three conditions; considerable increase of the perifascicular connective-tissue fibers, increase of the intrafascicular fibers of the same kind, and replacement of the muscular fibers by elastic fibrous tissue. These changes were accompanied or not by more or less thickening of the bladder walls, in which there was no useful muscular hypertrophy. The changes were not proportionate to the ages of the subjects, but they were always present, in the women as well as in the men. The act of micturition depends upon the musculature of the bladder which drives the urine out against resistance of different kinds, the mass of urine, closure of the neck, and the straightness of of the canal. In the normal condition this resistance is negligible, but in hypertrophy of the prostate it is very marked. In some cases the expelling force of the bladder alone is at fault, the resistance not being increased, as in prostatism in old women. Retention from a prostatic sarcoma in a young man would represent the other extreme of the scale, the resistance alone being increased. Prostatectomy removes the chief resistance and the remaining bladder muscle is strong enough to provide good micturition. Sometimes the muscle is so weak that after the removal of the prostate micturition is still defective, although these cases are very rare. Residual urine may persist after prostatectomy and then represents the clinical translation of the decrease of the expelling force of the bladder, due to the hyperplasia of the connective or elastic tissue in the muscular fasciculi of the bladder wall. In the great majority of cases, prostatism results from a diminu-

tion of the expulsive force of the bladder and an increase of the resistance of the passage of urine. The latter is most frequently the result of hypertrophy of the prostate, but as above shown it may occur in the absence of this cause.

THERAPEUTICS

UNDER THE CHARGE OF

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The Routine Application of Iodine to Eliminate Diphtheria Bacilli from the Throat.—STRAUCH (*Therapie d. Gegenwart.*, 1913, liv, 390) recommends the use of local applications of tincture of iodine to the tonsils as a routine measure when diphtheria bacilli are found in the throat a week after an attack of diphtheria. In 16 out of 50 cases, one or two applications of the iodine were sufficient to free the throat of the bacilli; in 20 others none could be found after three applications, and in 2 cases four applications were required. Although this method is not always successful the author thinks that it helps to control the further spread of the infection. The most striking results were obtained in chronic bacilli carriers some of whom were freed from the bacilli by a few days systematic use of the iodine applications.

Splenectomy in Pernicious Anemia.—EPPINGER (*Berlin. klin. Woch.*, 1913, I, 1509, 1572) believes that splenectomy may have a curative action whenever there is destruction of the blood from any cause. He has used this operation with good results in two cases of pernicious anemia. The spleen was not enlarged in either of these cases. In one of the cases of pernicious anemia the red blood cells increased from 1,160,000 to 4,900,000 in six weeks after the operation. Two cases of hemolytic jaundice were also much benefited by a splenectomy, the results amounting to clinical cures. Eppinger says that one of the marked indications of the result of the treatment was the diminution of the urobilin content of the stools after the removal of the spleen. He believes that the amount of urobilin in the stools is a most important indication of the destruction of red blood cells in the body. He cites some experimental work that, according to him, indicates that the spleen has hemolytic properties.

Salvarsan in Pernicious Anemia.—BOGGS (*Bull. Johns Hopkins Hosp.*, 1913, xxiv, 322) reports 4 cases of pernicious anemia, all of which showed favorable reaction to intravenous injections of salvarsan in the regeneration of the blood and relief of the symptoms. One was a most remarkable apparent cure of a patient in his fifth relapse, who was quite unresponsive to Fowler's solution and only showed a

very slight improvement after four months of sodium cacodylate injections. Under intravenous administration of salvarsan, in doses of 0.3 gm. every four weeks, he showed a steady rise in the blood count. The red cells, in sixteen weeks, rose from 500,000 to 5,000,000, the hemoglobin from 23 per cent. to 90 per cent., and the patient's general condition was much improved. This patient had no history of syphilis, and also had a negative reaction in serum and spinal fluid before any salvarsan was given. Another case of pernicious anemia was very responsive to salvarsan, his blood going from 1,100,000 to 3,400,000 red cells in twenty days after the first dose of 0.3 gm. salvarsan intravenously, eventually reaching 4,800,000 red cells with 85 per cent. of hemoglobin. This patient also gave no history of syphilis and Wassermann reactions in serum and spinal fluid were negative. However this patient relapsed quickly, only to rise to approximately a normal count again after two more doses. A blood picture, however, was never free from the qualitative changes of pernicious anemia. After several relapses and rallies over a period of one year, this patient died of an intercurrent bronchopneumonia. The other 2 cases, both negative for syphilis received but one injection each, and were greatly improved, with an average rise of 2,000,000 red cells when they left the hospital. Boggs thinks that his results and the results of other observers would certainly justify the further use of salvarsan in pernicious anemia with especial attention paid: (a) To the question of syphilis in the patient; (b) to the influence of salvarsan when given alone; (c) to the effect in cases refractory to arsenic; and (d) to the question of permanency of the results.

The Treatment of Syphilitic Affections of the Central Nervous System with Especial Reference to the Use of Intraspinal Injections.—SWIFT and ELLIS (*Arch. Int. Med.*, 1913, xii, 331), from their experience of the past two years, feel that 0.2 gm. or 0.3 gm. salvarsan is too small a dose, and that neosalvarsan given in the same relative amounts as salvarsan is much inferior to salvarsan. At present they give full doses of salvarsan—0.45 gm. to 0.5 gm. every two weeks, and in addition intraspinal injections of 30 c.c. of 40 per cent. serum, until the cerebrospinal fluid shows a normal cell count and a negative Wassermann reaction. (The technique of making the intraspinal injections and the method of obtaining the serum, which is obtained from blood withdrawn from the patient one hour after the intravenous administration of salvarsan, is fully described in the article.) Under this plan of treatment many of the cases are showing more rapid improvement than did those treated a year or more ago. Unfortunately their experience with general paresis is too limited to give definite results. One patient with early paresis and one or two others who are borderline cases between tabes and paresis have shown a rapid decrease in pleocytosis and a moderate decrease in the globulin, but the Wassermann reaction has been slower in showing a response. When one considers the anatomical difficulties in reaching the myriads of spirochetes that are present in the brain in this condition he is impressed with the necessity of prolonged and vigorous treatment. Another point brought out by the work here presented, is that the treatment of chronic syphilitic diseases of the central nervous system is not the administration of two or four intravenous injections of

salvarsan, or the exhibition of a certain amount of mercury and iodides. Each case presents a slightly different problem, and must be considered individually. Some respond much more rapidly than others but the object in all should be to obtain a persistently normal cerebrospinal fluid. Of course, it cannot be stated with certainty that a normal cerebrospinal fluid assures that there will be no further progress of the degenerative process. All that can be said is that as long as the cerebrospinal fluid gives evidence of a specific pathological process in the central nervous system, and there are specific therapeutic measures which will remove that evidence, these measures should be applied. Only when the fluid has become normal is it justifiable to discontinue the treatment and observations of the fluid should be continued so that at the first evidence of relapse treatment may be resumed. The method of intraspinal injection is not presented as a substitute for any of the accepted forms of treatment, but as an aid in attacking these severe infections. Swift and Ellis feel that there is definite evidence that this form of treatment has a curative action on the syphilitic process, and that, therefore, its combination with intensive treatment is required, as in rapidly advancing tabes or paresis, or where the disease has resisted other forms of treatment

Skin Rashes following the Administration of Atophan.—PHILLIPS (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1040) reports 5 cases where the administration of atophan was followed by the development of various types of skin rashes, resembling those rashes following the administration of antipyrin. The rashes produced were of various types—purpuric, urticarial, and scarlatinal form. Phillips therefore believes that this drug should not be given in the treatment of urticaria, as has been advised. Müller has called attention to the occurrence of a scarlatinal form of eruption in the case of a girl, aged twenty-three years. In this patient from 2 to 3 gm. of atophan were given daily in the treatment of arthritis. In the discussion of Müller's paper, Porges mentioned the fact that he had seen urticaria in cases in which atophan had been given.

The Effects of Colloidal Copper with an Analysis of the Therapeutic Criteria in Human Cancer.—WEIL (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1034) says, in brief, that the demonstrable reduction in size of a tumor of a kind not to be attributed to the natural processes of evolution of that tumor or of its associated lesions, is the one essential feature of effective therapeutic intervention. Weil says that the preparation described by Loeb as colloidal copper has been administered in 12 cases of malignant disease, in 8 of which the treatment was thoroughly carried out. The treatment resulted in most of the cases in the production of mild constitutional effects, such as fever, chills, nausea, some loss in weight, slight reduction of hemoglobin, and occasional albuminuria or hemoglobinuria. Chemical analysis of two tumors from treated patients failed to reveal the presence of copper, while in a liver obtained at necropsy it was present in appreciable quantity. Judged by certain clinical criteria, which have been adopted as a reliable standard of therapeutic effectiveness, the treatment has not appeared to exert a destructive action on the tumor tissue in any of the cases.

PEDIATRICS

UNDER THE CHARGE OF

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The Röntgen Rays in the Diagnosis of Obscure Abdominal Conditions.
—JOHN LOVETT MORSE (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1422), by a series of excellent case histories illustrated by radiographs explains the value of the Röntgen rays in the diagnosis of obscure conditions in the stomach and abdomen. In persistent vomiting after feedings the radiograph shows none of the test meal leaving the stomach in pyloric stenosis, or when due to spasm or disturbed digestion the stomach is shown empty or nearly so after two hours. In cases of recurrent vomiting and abdominal pain, either singly or in combination, the Röntgen rays furnishes evidence of the greatest importance. In the case of a boy of six years, subject to repeated attacks of vomiting with abdominal pain, and whose appendix had been removed without benefit, the radiographs showed marked splachnoptosis, the lower border of the stomach being below the level of the iliac crests. In a case suggestive of stone in the bladder in a girl subject to severe attacks of abdominal pain the radiographs taken at various intervals after a test meal showed the gastro-intestinal tract and its functions normal down to the transverse colon which had sagged down in a V-shape and reached nearly to the pubis, thus explaining the symptoms as due to inference with intestinal peristalsis. The radiographs also determine the existence of adhesions in the abdomen as in the case of a girl, aged fifteen years, with attacks of severe abdominal pain, where the radiographs showed prolapse of the cecum into the pelvis with the ascending colon bent sharply downward on itself before joining the transverse colon. Every picture taken showed the same relation of the colon to the cecum and a subsequent laparotomy showed adhesions in the places shown by the radiographs. This method is of great value in determining delay in the passage of food through the gastro-enteric tract, and, if so, where the delay takes place. Radiographs of the abdomen after a bismuth enema show accurately the position of the large intestine.

Appendicitis Caused by Thread-worms Simulating Meningitis. — R. N. H. ANGLIN WHITELOCKE (*Brit. Journ. Child. Dis.*, 1913, x, 296) reports the case of a girl aged over five years with an almost positive tuberculous history who was admitted to hospital with the diagnosis of meningitis. The symptoms were fever, rapid pulse, marked converging strabismus, contraction of both pupils, and photophobia. She had urinary incontinence; any attempt at drinking brought on immediate vomiting, and she screamed out when apparently dosing. This condition continued for two days when rigidity and tenderness over the right rectus muscle was noticed, with flexion of the right thigh. On operation an inflamed appendix was found packed full of thread-worms. Living worms were seen emerging through a

minute perforation at the tip, and worms were found free in the peritoneal cavity. After the operation the symptoms disappeared and the patient entirely recovered. One of the interesting points is the imitation of a true organic nerve lesion by reflex irritation produced by active animalcules wriggling about on an exquisitely sensitive peritoneal surface.

The Diphtheria Bacillus and Scarlatinal Infection.—T. SHADICK HIGGINS (*Brit. Jour. Child. Dis.*, 1913, x, 481) reports the results of a two years' study of the association of the diphtheria bacillus with scarlet fever. Observations appear to show a connection between the presence of this germ with the persistence of scarlatinal infectiousness, especially with the question of return cases. Rhinitis is common among patients who produce "return cases," and the diphtheria bacillus is very frequently present in such conditions. Out of 379 primary cases of scarlet fever which caused return cases, 145 or 38 per cent. showed positive swabs for the diphtheria bacillus. It was determined that most of the positive cultures contained the true diphtheria bacillus, as, for instance in a complete bacteriological test of 22 positive cultures of diphtheroid bacilli, the true bacillus was found in 13 or 60 per cent. It was also found that 25 per cent. of all houses where return cases occurred had received home from hospital a primary case from whom the bacillus diphtheriæ could be recovered. Out of 102 patients whose return from hospital did not give rise to return cases only 7 per cent. showed positive cultures from the nose and throat of true diphtheria bacilli. Out of 99 normal school-children, who had never had either scarlet fever or diphtheria, 7 per cent. showed positive cultures of the diphtheria bacillus, of which only a minority were fully virulent. In one school comparatively free from scarlet fever only two children showed true bacilli, whereas in the other school from which the other half of the subjects had been taken and where scarlet fever was prevalent five children showed the bacillus. These results seem to show that the presence of this diphtheria bacillus in cases of scarlet fever tends to prolong the scarlatinal infectiousness.

The Ammoniacal Diaper and Its Correction.—THOMAS S. SOUTHWORTH (*Archiv. of Pediatrics*, 1913, xxx, 732) discusses the ammoniacal diaper as a clinical sign and notes the absence of information on this point in text-books of pediatrics. In a series of cases showing strongly ammoniacal urine Southworth found that the feedings contained a high percentage of fat and that there was usually a disturbance of the bowels and indigestion. In these cases a short reduction of fat in the feedings resulted in great amelioration or entire disappearance of the ammoniacal odor in the diaper. Increasing the fat usually brought a return of the ammoniacal condition. Malt soup in which a very low fat percentage is compensated for by a relatively high carbohydrate percentage was often found of great value. The etiology of the ammoniacal condition is explained by the conclusions of Keller and Czerny that there is present an excess of unoxidized acids in the body, that the available supply of fixed alkalis is not sufficient to neutralize this excess and ammonia takes their place, forming ammonia salts with the acids which will be excreted by the urine. Fats cause

most of the trouble by the formation of fatty acids. The therapy of excessive ammonia excretion is to prevent improper formation of acids by reducing the fat percentage in the feedings and so promote better fat metabolism, and to prevent undue loss of alkalies by administration of alkalies by mouth, preferably calcium and magnesium. An odor of ammonia on the diaper, therefore, is presumably traceable to an actual or relative overfeeding with the fat of cow's milk.

OBSTETRICS

UNDER THE CHARGE OF

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The Frequency of Puerperal Fever.—It is sometimes interesting to form an idea of the frequency of puerperal fever in modern times. LOEB (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 3) from 1881 to 1910 has obtained the statistics from Bavaria, and finds that in 1000 women dying from various causes, in 1881 that 7.4 per cent. died of puerperal sepsis. The lowest death rate was from 1896 to 1900, or 4.9 per cent.; and the most recent, 1906 to 1910, was 5.1 per cent.

BAISCH (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 4) contributes an interesting paper upon the endogenous cases of puerperal septic infection, dividing them into two classes, in one of which exogenous bacteria gained access to the body, while in the other endogenous germs became pathogenic. He finds that a properly conducted digital examination does not predispose to infection, while vaginal douches, the introduction of foreign bodies, and operative procedures, are favorable for infection. That septic death may occur without the involvement of the genital organs is shown in a case cited, where twenty days after labor a typical thrombosis developed in the right leg with signs of infection. At autopsy the pelvic veins were normal, as were also the uterine sinuses. The veins of the right lower extremity showed thrombosis, which could not be traced to the genital organs. Bumm's interesting cases are cited, in which three patients after spontaneous labor had severe streptococcus infection; two of these before labor had used a bathtub in which there had been washed a laboratory glass which had contained streptococci. The third patient had used linen which had come from an infected and isolated portion of the hospital. Sepsis from infected cotton placed in the vagina has been observed, and also from infection of the tonsils and lymphatic glands. In order to make a correct diagnosis in a given case, the body must be subjected to a thorough postmortem examination.

KÖHLER (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 2) describes a cutaneous reaction obtained in puerperal sepsis by

using streptococci antigens. This reaction was limited to those patients in whom the streptococcus was found in the blood. It is absent in fatal cases, although streptococci may be present in the blood.

SCHWAB (*Zentralbl. f. Gynäk.*, 1912, xliv) reports an interesting series of obstetric operations in private houses, with a view to determining the frequency of infection. Lysol was the antiseptic employed, and the patients were prepared by external cleansing with this agent. The hands of the physician were cleaned with soap and a brush, and lysol and alcohol. Gloves were not used. There were 63 forceps operations, 17 versions, 6 extractions by the breech, 7 induced labors, 6 craniotomies, 3 embryotomies, and 1 dilatation with Bossi's dilator. In 1 patient in eclampsia where labor was induced the placenta was manually extracted. Labor was induced in 7 patients without the occurrence of fever; the 6 breech extractions were likewise successful, and the 3 embryotomies; and the puerperal period was undisturbed. One of the patients died after perforation from septic infection, and the infection could not be traced; one patient died of infection after version. Among 63 forceps operations there were 3 deaths of children, but no maternal deaths. In the cases which had fever the source of the infection could be traced outside the body of the patient.

The subject of opsonins and vaccines in puerperal septic infection is still under discussion. In *Surgery, Gynecology, and Obstetrics*, December, 1912, MEDALIA and WALTON, while they cannot draw definite conclusions from their work, believe that the opsonic index is of value in determining the severity of infection and the patient's resistance. It cannot, however, decide that a given streptococcus is virulent, or is not. The difficulty of applying this test in ordinary practice would limit its use to hospitals and laboratories. They also believe that vaccine treatment is of positive value.

BRINDEAU (*Archiv. mens. l'Obstet.*, March, 1912) has treated puerperal infection with cultures of the lactic acid bacillus. He had good results in treating infected wounds, especially those of the perineum and vulva. These wounds cleaned rapidly, and this method may be used with advantage in preparing patients for secondary operation.

ROWLETTE (*Jour. Obstet. and Gynec. of British Empire*, June, 1912) has treated 54 patients, among whom a bacteriological diagnosis was made in 39. As soon as the bacteriological diagnosis was made a dose of vaccine was administered. In regard to treatment, 2,500,000 cocci were given streptococcal cases as a beginning. The vaccines were made from fresh twenty-four-hour cultures, and sterilized by the addition of 1 per cent. lysol in normal salt solution. A second dose was given forty-eight hours after the first, and this was repeated until the temperature and pulse had become normal, when one final dose was administered. This was afterward increased to 5,000,000, and occasionally 7,500,000. Usually from 20,000,000 to 25,000,000 cocci were given when the streptococcus was the infective agent, and in one case as many as 50,000,000. The injections were made in the arm or forearm, under the skin, with an ordinary hypodermic needle. A circumscribed flush about the puncture usually developed. There were 31 cases of streptococcal infection, the number of inoculations varying from 1 to 9, the average being 3.3. His experience shows that vaccines in small doses can do no harm, and that in the great

majority of cases they do good. An immediate and remarkable improvement is often observed. Autogenous are better than stock vaccines, and often are rapidly successful when the latter has failed. Antistreptococcus serum when given simultaneously with the vaccine, increases its effect.

In the *British Medical Journal*, July 6, 1912, JORDAN treats of puerperal sepsis and the vaccine treatment. He reports 15 cases treated by vaccines. There were 5 fatal cases where autopsy proved the correctness of the diagnosis. His cases presented the usual complication of septic infection. He would use biniodide of mercury, 1 to 1000, or local antiseptics about the perineum and genital tract.

AHLFELD (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxxii, Heft 1) is convinced of the value of alcohol locally as an antiseptic for the prevention of sepsis. If used after a thorough scrubbing with soap and water and biniodide of mercury solution, he believes that efficient antiseptics can be obtained.

GYNECOLOGY

UNDER THE CHARGE OF

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Acromegaly following Bilateral Oöphorectomy in an Adult.—In view of the extreme rarity of the development of anything suggestive of a true acromegalic condition following the removal of all ovarian tissue in an adult, a case recently reported by GOLDSTEIN (*Münch. med. Woch.*, 1913, lx, 757) is of some interest. The patient was forty-eight years of age, the eldest of a family of seven, all her brothers and sisters being healthy. In 1903 the uterus and both adnexa were removed on account of menstrual disturbances, associated with multiple myomas. The patient had always been of a rather large build, with heavier bones than the other members of the family, but in the year following operation there developed a gradual but marked increase in size of the entire body, this being due, as was demonstrated by the x-ray, primarily to a thickening of the bones, especially of the extremities. The face became broader also, and the chin more prominent; this process was accompanied by subjective symptoms, such as vertigo, great sensitiveness to slight variations of heat and cold, vague pains, palpitation, etc. Careful Röntgenological study failed to reveal any increase in the size of the hypophysis. There is no doubt in Goldstein's mind that the condition is a true acromegaly, coming on subsequent to the castration. In view of the large numbers of double oöphorectomies that are performed, however, and the very great rarity of this condition developing subsequently, it can hardly be assumed in this instance that the removal of the ovaries *alone* was the cause of the acromegaly, notwithstanding the well known

trophic influence apparently exerted by these glands upon osseous development. The patient was from birth of larger and coarser build than her brothers and sisters, so that it seems probable that she had a congenital tendency to gigantism; in other words, that the delicate balance between the secretions of the ductless glands governing stimulatory and inhibitory functions with respect to growth were abnormally unstable, so that the ablation of one important set of glands of internal secretion—the ovaries—was sufficient to upset this balance and to cause a hyperactivity of certain other glands, perhaps chiefly the hypophysis, without, however, causing a demonstrable increase in the size of this.

Is Uterine Carcinoma Ever Cured by Curettage?—An interesting case, which brings up this question, is reported by HESS (*Deutsch. med. Woch.*, 1913, xxxix, 1038). A woman, aged forty-one years, presented herself for treatment, complaining of loss of weight and strength, hemorrhage lasting for three months, and foul discharge. No tumor was palpable, but microscopic examination of tissue removed by curettage showed a typical adenocarcinoma corporis uteri, this diagnosis being confirmed by a number of thoroughly competent pathologists. Radical operation was therefore advised, but was absolutely refused by the patient, whose sister had recently died following operation for an abdominal cancer. The patient has been kept under observation for four years; the hemorrhage and discharge have entirely ceased, she has gained in weight and strength, and is now apparently in perfect health. In view of the clinical symptoms and the microscopic examination of the curettings there can be no reasonable doubt that the case was really one of beginning carcinoma of the uterine body. To determine just what has taken place, is, however, extremely difficult. Four chief possibilities come into consideration: (1) Has the malignant tumor undergone spontaneous retrogression and eventual disappearance? (2) Is the cure only apparent; i. e., is the malignant process still present in the body in a latent condition, causing at present no symptoms whatever, but to reappear at some future time? Such cases have been reported. (3) Was the small area of beginning malignancy confined solely to the endometrium and completely removed by the curette, leaving nothing but normal tissue behind? (4) Was the major portion of the tumor removed, and the scattered remnants so damaged that they fell an easy prey to the hemorrhage caused by the curettage, undergoing lysis and ultimate disappearance? Hess admits his inability to determine by which of the processes the clinical result has been brought about, but thinks that several of them may have acted together. In a note appended to the above report, a somewhat similar case is reported by v. Hanse-mann, who was one of the pathologists to confirm the diagnosis. In this instance, a curettement was done upon a girl, aged seventeen years, on account of a suspicion of malignancy. The curettings showed an unmistakable squamous-cell carcinoma of the uterine body; the uterus was therefore removed, but serial sections of practically the entire endometrium failed to reveal a single carcinomatous area. A third case of this nature is reported by STRATZ (*Zentralbl. f. Gyn.*, 1913, xxxvii, 1141). The patient had a constant fear of develop-

ing uterine cancer, from which disease her mother had died; she had therefore had a curettement performed every two years for microscopic diagnosis. About the third or fourth time the tissue removed showed definite malignancy, the diagnosis being confirmed by Ruge, but no trace of carcinoma could be found in the extirpated uterus, even after the most careful search. Although these 3 cases, and other occasional ones that have been reported in the literature, seem to indicate that in exceptional instances a simple curettage may be really curative of cancer of the uterine body, such instances are so exceptional that great harm would be done, as all the authors quoted emphasize, were confidence to be placed in its occurrence; such cases are interesting curiosities, but are in no sense to be considered as justifying a retreat from the universally accepted principle of radical removal of carcinomatous tissue when this is possible.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Traumatic Glaucoma.—C. and H. FROMAGET (*Annal. d'Oculistique*, January, 1913, p. 1) have made an interesting study of the occurrence of glaucoma after contusions of the eyeball without rupture of its coats. They conclude: that such traumatism occasionally, though very rarely, determines an acute glaucomatous condition which may immediately follow the injury or be delayed several weeks. This condition differs in nowise clinically from ordinary idiopathic acute glaucoma; accordingly they designate it as *essential traumatic glaucoma*. A second variety whose clinical identity with spontaneous glaucoma is not so well established, is observed to follow post hemorrhagic traumatisms; of this there are two forms: in one the hypertension is the essential factor, the hemorrhage being slight; in the other there is present with the hypertension a veritable inundation of the globe with blood. A third variety which may be termed symptomatic or false glaucoma occurs, in which the glaucomatous state is a sequel to other lesions, especially luxations or subluxations of the lens, or tears of the ciliary region with more or less extensive ruptures of the zonula. The latter make up by far the most numerous of the cases published under the name of traumatic glaucoma. The lesions to the lens system in these cases being at times difficult of diagnosis, may escape recognition and the case come to be regarded as one of pure glaucoma. Nothing can be affirmed as to the identity of origin

between a glaucoma provoked by traumatism and the so-called spontaneous form, depending as it does upon factors for the most part unknown, and which according to present views, appears to constitute a true morbid entity by itself.

"Angiopathia Retinae Traumatica."—Under the above title, PURTSCHER (*Centralbl. f. p. Augenhk.*, January, 1913, p. 1) describes a little known but characteristic type of retinal disease following severe trauma of the skull and certain definite varieties of trauma affecting the body as a whole, compressing the same and causing increased tension within the cranium. The phenomena in question consist of shining white spots situated in the innermost layers of the retina, appearing some days after the injury; the spots are of variable size and number, are grouped about the entrance of optic nerve and macula and follow, in general, the course of the large retinal veins; they occasionally accompany the smaller venules also. The papilla usually appears entirely normal, or if presenting signs of papillitis, the latter seem to be independent of the spots. As to the cause of these appearances in the retina, Purtscher is strongly inclined to the view that they are the consequences of lymph extravasations within the retinal tissue due to *acute* increase of tension within the cavity of the cranium; (chronic increase gives rise to choked disk, as has been long known); not that recently extravasated lymph can itself be recognized by the ophthalmoscope directly, but that the spots represent nutritive disturbances occasioned by the lymph, laden as it is with toxins elaborated by the crushed portion of the cerebral mass, as suggested by Liebrecht in commenting upon a case of his own. In any event the reporter raises the question in how far the lymph channels of the eye, especially of the retina, are concerned in the production of a variety of ophthalmoscopic pictures affecting the retina and optic nerve—questions to be determined by careful examination of analogous cases, especially of such as come to autopsy.

Clinical Researches with Schiøtz's Tonometer.—FOURRIERE (*Annal. d'Oculist.*, January, 1913, p. 26) summarizes the observations of himself and others of the results of tonometric measurements of the normal eye with Schiøtz's Tonometer. As to the normal tension, he finds that there is no one definite normal tension; in a great number of cases the instrument registers 18 mm. of Hg., but the tension has been found to vary in health between 12 and 27 mm. Stock makes the opposite observation that in eyes whose normal tension is as low as 12 mm., for example, 20 mm. may indicate hypertension. This circumstance explained the evolution of glaucoma in some cases showing an apparently normal tension. Both eyes normally show the same tension, though a difference amounting to 11 mm. has been reported. Age appears to be without influence upon the tension. The same is true of the arterial pressure. The hour of the day seems to exercise no influence, neither do differences of refraction. Grönholm finds that dim light, favoring mydriasis as it does, tends to raise the tension slightly. The same author finds that accommodation most frequently causes lowered tension; movements of the eyes are without effect. Ocular massage has a decided influence in lowering the tension,

As to medicaments (holocain, cocain, atropin, novocain, stovain, pilocarpin, eserin) all have been found to exercise a very feeble action upon the tension of a normal eye. The same collyrium produces now a slight hypertension and again feeble hypotension without obvious reason for the difference. Of these various remedies the effect of eserin appears to be the most constant in depressing the tension slightly.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Protective Inoculation by Leukocyte Extract.—Hiss (*Jour. Med. Research*, July, 1913, xxviii, No. 2) has for the past five years or more been dealing with the effect of leukocyte extract as a remedial measure. He selects certain diseases which are not specially amenable to serum treatment, and suggests that in these diseases the body defence is largely cellular, it may be by phagocytosis, by digestion, by neutralization or by destruction of poisons, or by all of these combined. If this were so, it would be useful to assist the leukocytes by supplying them with additional weapons in the shape of materials not ordinarily given up to the plasma or serum, which materials being diffusible, would be more efficacious than intact leukocytes, because more diffusible and immediately available for the use of the fatigued or exhausted leukocytes of the body. The idea of immunity here suggested, is that there are, in the leukocytes, agents which are not normally given out to the plasma, for the use of the body at large, but which remain in the leukocytes for their individual benefit or protection. The mode of preparation is that rabbits are injected intrapleurally with sterilized aleuronat. The copious and very cellular exudate resulting is removed, centrifugated, and the leukocytic sediment diluted, examined as to its sterility, and kept for use. Experiments have been repeatedly made upon animals suffering from infections of staphylococcus, streptococcus, pneumococcus, typhoid, dysentery, meningococcus, and cholera. In practically every case, treated animals withstood infection better than controls, and in some cases the results were very striking. It often appeared that the animals treated were intoxicated to a greater extent after the leukocytic extract was used than were the controls, but the ultimate results seen in such animals left no doubt in the observers' minds of the beneficent effects of the procedure. They consider that it is in no wise a question of the extract stimulating general leukocytosis, nor yet of bacterial destruction, but rather that a direct effect is produced upon the poisons generated. The application of this method of treatment in human subjects has already been made with satisfactory results in

meningitis (previously published), pneumonia, erysipelas, and other infections, and has proved so beneficial as to render the outlook hopeful that there is here a therapeutic measure that ultimately will prove very useful.

Some Unusual Infections.—RUSK and FARNELL (*Univ. of Calif. Publications in Pathol.*, vol. ii, No. 5) report 2 cases of granulomatosis, both of which terminated by an infection of the meninges, the fluid obtained by lumbar puncture indicating the diagnosis. One of the patients had suffered from a skin infection caused by the organism—an oidium—and the microscopic examination of the organs showed, in general, overgrowth of granulation tissue, with giant-cell formation, and occasionally abscesses. In one of the two individuals, the granulation processes in the lung were followed by cavity formation. SPILLMANN and JEANNIN (*Bull. d. l. Soc. franc. d. Dermatol. et de Syphilog.*, April, 1913) describe a dermatomycosis caused by one of the conidiospores, entitled *Carethropsis hominis*. This organism has not hitherto been known to be pathogenic; the disease existed superficially on the arm. CHOMPRET and IZARD (*Ibid*) report a case of actinomycosis of the temple with fistula formation and trismus, due to implication of the temporal muscle; the infection had spread from the mouth cavity. PAUTRIER, BELOT, FERNET and DELORT (*Bull. d. l. Soc. franc. d. Dermat. et d. Syphilogr.*, February, 1913) report a typical case of mycosis fungoides, which appeared in various parts of the body. Under treatment it became better, but relapsed, and during the period in which the superficial lesions were becoming healed with scarring, a series of tumors appeared which proved to be sarcomatous.

Glands of Internal Secretion and the Growth of Sarcoma.—KORENTECHESKY (*Vratch. Gaz.*, 1913, xx, 489) studied the question of the influence of the glands of internal secretion upon the growth of sarcoma, and found a certain connection between the processes. He subjected dogs to ablation of the thyroid, to castration, and to both operations, and subsequently injected emulsion of sarcoma cells, controlling his experiments throughout. The tumors grew most rapidly in animals only strumectomized or only castrated, more slowly in animals which have been subjected to both. In castrated dogs, the tumors resorb quickly, while in controls and in dogs submitted to both operations, resorption begins after three months. In strumectomized animals, however, resorption is inappreciable. It appears to the reviewer that the experiment may not be so uncomplicated as it appears, as questions of nutrition and the influence of the nervous system ought to influence the observations.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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ORIGINAL ARTICLES

THE ETIOLOGY AND PATHOGENESIS OF BRONCHIECTASIS.

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SINCE the young French student Cayol first called the attention of his preceptor, Laennec,¹ to a bronchiectatic lung, many theories have been advanced as to the etiology and pathogenesis of this interesting condition. Clinically it is rare, though relatively common in the autopsy room in association with phthisis, as is pointed out by Fowler.²

We are, therefore, rather fortunate in being able to report 4 cases which occurred among 967 medical admissions to the University Hospital: 3 of them were under twenty years of age and 1 over forty. In Lebert's series of 83 cases, 47 per cent. occurred before and 53 per cent. after the fortieth year, while in Acland's series of 60 the percentages were 77 and 23 respectively. The predominance of the male sex must be largely due to the greater number of male admissions to the general hospitals from which the majority of the reports are drawn.

Anatomical and clinical classifications have been advanced by almost every writer on the subject. The generally accepted anatomical one includes three groups: (1) A regular or cylindrical bronchiectasis, in which there is dilatation of the tubes toward the periphery of the lung, and (2) a fusiform type, in which, in addition

¹ De l'Auscultation Mediate, 1819, i, 124 (Brosason et Chaudé, Paris).

² Diseases of the Lungs, by J. K. Fowler and R. J. Godlee, 1898, 123 (Longmans, Green & Co., London).

to the above there is a dilatation at the periphery resulting in a bulbous termination; (3) the globular or sacculated type, in which the dilatations are strictly terminal.

Of the many clinical classifications, in our opinion that of Hoffmann³ seems the most scientific. He recognizes four groups: (1) Inflammatory, (2) vicarious, (3) congenital, and (4) ateleectatic.

1. The inflammatory group comprises the vast majority of the cases, and is nearly always of the saccular type. Two main subdivisions can be made: one associated with stenosis, and the other, the "indurative bronchiectasis," in which a thickened membrane attaches the portion of the lung affected with the ectasis firmly to the thoracic wall.

2. Vicarious or substituted type, in which the dilatation is always cylindrical. "When a portion of the lung has become inaccessible to the air and its volume is reduced, the traction excited on the adjoining tissues during inspiration will cause them to make an attempt to fill the space." The powerful pull of the muscles which dilate the thorax and so act on the lungs will be unable to expand the impermeable portions, but will expand other ones. According to the position and circumstances, this may affect the alveoli or the bronchi, and thus arise vicarious emphysema and bronchiectasis; hence, the not infrequent association of the two conditions. The mucous membrane seems thinned like a serous membrane. No inflammatory processes take part in the disease; it is a true emphysema of the bronchi, but it has little or no importance clinically.

3. Congenital bronchiectasis was first described by Grawitz⁴ and subsequently by Neisser.⁵ Grawitz recognized three varieties: (a) A universal ectasia, in which there is a large common cavity with numerous recesses; (b) telangiectatic, in which only the smaller bronchi are attacked. These may be regarded as a malformation or as the result of some intra-uterine disease, as syphilis. The morbid process is usually confined to one lung, which may present a cyst with a central space branching into a peripheral set of intercommunicating secondary and tertiary cysts, with serous contents. (c) Grawitz described a third variety, with numerous separate cysts formed on the bronchi of the third and fourth order, some communicating with the bronchial lumen and others closed. Goitre was found associated with this malformation. (d) Lastly, congenital bronchiectasis may be due to a dermoid growth invading a bronchus, as described by Cyril Ogle.⁶ These congenital cases are comparatively rare, and have never been seen by the writer.

³ Diseases of the Bronchi, Lungs, and Pleura, 1903, 178; Nothnagel's Practice (W. B. Saunders & Co., Philadelphia and London.) (Edited by J. H. Musser).

⁴ Archiv f. Path. Anat., Berlin, 1880. lxxxii, 217.

⁵ Zeit. f. klin. Med., 1901, xlii, 88.

⁶ Trans. Path. Soc., London, 1897, xlviii, 1909.

4. Atelectatic: Ewart⁷ also speaks of the atelectatic variety of Heller, in which there is an abnormal growth of the bronchial cartilages, together with remnants of the unexpanded non-pigmented fetal lung tissue, with epithelium of the pavement variety.

ETIOLOGY. Let us first consider Fowler's classification of the various conditions, which may be responsible for the development of bronchiectasis.

A. *Intrinsic*, that is, conditions acting directly through the bronchi.

1. *Acute and Chronic Bronchitis*. Bronchial catarrh is regarded by the majority of writers as the chief and earliest etiological factor. The special action of the catarrh consists in the mechanical plugging of the bronchioles. Juergensen⁸ believes that long-standing bronchial catarrh may under certain conditions produce a growth of the interstitial connective-tissue of the lungs, which further favors the origin of bronchiectasis. In children the bronchiectasis may run a very acute course, and the finest bronchi may undergo dilatation, a condition termed bronchiolectasis. It has been fully described by Fowler, Walter Carr,⁹ and others in England, but has received scant attention in America. The isolation of the bacillus influenzae by Leichenstern and M. Beck of Europe, and by Lord¹⁰ and Boggs¹¹ of this country, in a large proportion of cases of bronchiectasis suggests the important role played by influenzal bronchitis in the etiology of bronchiectasis.

2. *Bronchial Stenosis*. Bronchial stenosis may result from (a) gumma of the bronchi; (b) tuberculosis; (c) the pressure of an aneurysm or a tumor; (d) a foreign body.

(a) The role of syphilis in bronchiectasis and other pulmonary diseases has been much underestimated since the days of Laennec, according to Bouchut and Dujol.¹² They refer to 5 cases of bronchiectasis of Laurent and Guerin, in all of which the Wassermann reaction was positive, and give in detail one case of their own in which other syphilitic lesions co-existed. L. A. Conner,¹³ in a critical review of syphilis of the trachea and bronchi, found among 56 autopsies dilatation of the trachea three times and dilatation of both bronchi in 9 cases. He asserts: "The surprising thing is not that they occasionally occurred but that they should have been found so infrequently. In not more than 20 per cent. of the cases of permanent stenosis did bronchiectasis occur." It seems evident, therefore, that the tracheal or bronchial stenosis is not the chief determining cause of the bronchiectasis found. "Much more potent

⁷ Allbutt and Rolleston's System of Medicine, 1909, v, 127 (McMillan & Co.)

⁸ Handbuch der speciellen Pathol. u. Therap., 1877, H. Ziemsen, Band v, i, 286 (Liepzig. F. C. W. Vogel).

⁹ Practitioner, 1891, xlv, 87.

¹⁰ Boston Med. and Surg. Jour., 1902, cxlvii, 662, *ibid.*, 1905, clii, 537 and 574.

¹¹ AMER. JOUR. MED. SCI., 1905, cxxx, 902.

¹² Rev. de Med., 1912, xxxiii, 585.

¹³ AMER. JOUR. MED. SCI., 1903, cxxvi, 57.

factors are the changes occurring in the bronchial wall and in the adjacent lung tissue, by which the muscular and elastic tissue of the bronchi upon which their strength and resilience depend is replaced by inflammatory tissue." Osler and Gibson¹⁴ speak of three pathological types of syphilitic bronchiectasis: (1) With an interstitial pneumonia of the lower lobes, adherence of the pleura with general dilatation of the bronchi and cavity formation; (2) cases with a large single cavity in the upper lobe, with smooth thick walls; (3) cases which follow stenosis of the bronchus. In children certain cases run an acute course and reveal at autopsy a picture identical with that described by Grawitz as congenital bronchiectasis. While the "honey-comb" appearance of a bronchiectatic process limited to one lobe is usually due to syphilis, Weill and Gardere¹⁵ have recently reported two cases in children of three and ten years respectively in which the honey-comb lung was due to tuberculosis. The important conclusion to be drawn from the above observations is that syphilis plays an important role in the etiology of bronchiectasis and should always be excluded in a given case.

(b) Tuberculosis: Tuberculous processes are so slow that the lung can accommodate itself to the altered conditions, though stenosis may occur as the result of erosion through the bronchial wall. Chevalier Jackson¹⁶ has seen 6 cases illustrating this possibility. The following case belongs in all probability to this category.

CASE I.—Pulmonary tuberculosis (?); bronchial stenosis; bronchiectasis. M. D., aged forty-five years; laborer. Admitted March 13, 1913. Not referred. Clinical No. 881. Complaints: "Spells of coughing."

The family history was negative for tuberculosis. Patient was a day laborer, and had worked much recently in dusty atmospheres, shovelling coal. He had used alcohol to excess for years. He admitted gonorrhea at thirty-two years, at which time he had a single sore on the penis, for which he took local treatment and one bottle of medicine, and never developed any secondaries. He denied absolutely ever having been sick in bed in the past twenty years, but finally admitted to having some cough, with slight amount of sputum, for the past ten or fifteen years. Ten years before the onset of the present illness he had a pleurisy of the left side, which lasted for a day or two. In October, 1912, during a paroxysm of coughing, something "seemed to break" in his chest, and the sputum for a day or so following was especially offensive.

The present illness dated from January 17, 1913, when, following

¹⁴ System of Syphilis (Edited by D'Arcy Power and J. Keogh Murphy), 1909, III, vii, (London-Oxford Med. Pub.).

¹⁵ Lyon Méd., 1912, cxviii, 1221.

¹⁶ Jour. Amer. Med. Assoc., 1912, lix, 1123.

a prolonged spree, he developed cough and sputum. The cough was paroxysmal in character, associated with change of posture, and was especially frequent in the early morning. The sputum was profuse, and was so offensive as to be noticed by his fellow-workmen. It was usually yellowish in character, but occasionally had been blood-streaked. Since the present onset the patient had had chills, fever, and night sweats, and, though not confined to bed, he had not been at work. The appetite had been good. He fell from an average weight of 155 pounds to 133 pounds.

Physical examination revealed a well-developed and fairly well-nourished man, with flushed face, due in part to cyanosis and in part to dilatation of the venules. There was also cyanosis of the ears, lips, and finger tips, but no clubbing, though slight incurvature of the nails. The breath was extremely offensive, and of the same odor as the sputum. The thorax was of the emphysematous type, with somewhat restricted expansion, but no apparent flattening or retraction. Litten's sign was present on both sides. The percussion note was hyperresonant, except in the lower left interscapular region and base, where it was distinctly dull. Over this area vocal fremitus was diminished, and the breath sounds enfeebled and accompanied by numerous medium moist rales and high piping sonorous and sibilant rales. The heart revealed a normal area of dullness without displacement. The sounds were loud, regular, and clear, and there was no special accentuation of either second sound. Pulse was 84, large, full, and regular in force and rhythm. Blood pressure, 108 mm. (Faught); vessel wall distinctly palpable. The abdomen was round and soft. The liver was pushed somewhat downward by the emphysematous lungs, so that the relative cardiac dullness reached 5 cm. below the costal border in the right parasternal line. The edge of the spleen could not be felt. Hemoglobin, 70 per cent. (Sahli); red cells, 4,700,000; white cells, 16,600. Differential count: Polynuclears, 81 per cent.; lymphocytes, 15 per cent.; large mononuclears, 3 per cent.; transitionals, 1 per cent. Wassermann test was negative on two occasions. Von Pirquet test was positive. The urine contained very slight traces of albumin and an occasional hyaline and granular cast. The sputum varied from 165 to 300 c.c. in amount, and was yellow, purulent, separating into three layers, and having a distinctly sweetish, offensive odor; on one or two occasions it contained elastic tissue; repeated examinations, however, failed to reveal acid-fast bacilli. Cultures were negative for *Bacillus influenzae*, but numerous staphylococci and streptococci could be isolated. The skiagram revealed in the lower left back a distinct shadow corresponding to the area of impairment (Fig. 1). There was no evidence of infiltration of either apex. The patient on admission was running a high, irregular fever, which persisted for some two or three weeks, and was associated with a progressive loss in weight. Hypodermic injections of guaiacol

cleared up the offensive odor of the sputum, and the daily inhalations of creosote also for a time caused considerable improvement in the patient's well-being, though the amount of sputum remained excessive.

On April 23, on account of another exacerbation of fever, sweats and chills, and increase in the area of dulness, an aspirating needle was introduced into the eighth left interspace in the scapular line. After considerable resistance was overcome the needle was steadily introduced into the lung substance, and though nothing could be aspirated into the Ricord syringe, after withdrawal of the needle



FIG. 1.—Case 1. Pulmonary tuberculosis; bronchial stenosis; bronchiectasis.

a small particle of thick, yellowish pus was found in the needle, which, in smears, showed numbers of pus cells and many bacteria, diplococci, and small bacilli. On April 26 a second puncture in the ninth interspace closer to the vertebral line was performed, but with absolutely negative results, though on this occasion a needle with a still larger lumen was used. Another skiagram revealed a more definite shadow corresponding to the increased area of dulness.

Under local anesthesia, on May 2, Dr. L. W. Dean introduced a bronchoscope into the left bronchus. This revealed, fourteen

and a half inches from the upper central incisor teeth, red granulation tissue and a cicatricial stenosis, which after some difficulty was eventually dilated, resulting in the evacuation of two ounces of foul, thick pus. The cavity was thoroughly cleansed, with cocaine and adrenalin, and the walls carefully examined. The latter were covered with red granulations, but no trace of a foreign body could be found. The drainage afforded by this procedure was followed by a temporary improvement in the patient's condition. Before subsequent dilatation could be carried out the patient left the hospital without permission.

(c) Many cases of thoracic aneurysm or mediastinal tumor exerting sufficient pressure on a main bronchus to bring about a certain degree of stenosis have been observed. In some of these cases bronchiectasis may result, as was frequently observed by Osler, who has termed it "aneurysmal phthisis."

(d) *Foreign Bodies*. The presence of a foreign body with partial obstruction of the bronchial lumen is not an infrequent cause. Cohn¹⁷ found experimentally that dilatation usually occurs around the foreign body and not behind it. It is the continual irritation that causes the inflammation and ulceration and leads to a cavity formation. The local irritant acting continuously causes a peribronchitis which, extending from the site of the foreign body to the bronchi, favors in a special way the formation of bronchiectasis. Hoffmann states: "I must add that foreign bodies are too little considered as causes of bronchiectosis. We have cases enough in which the course and all the circumstances did not suggest the idea that a foreign body could have passed into the lungs and where the autopsy first showed to the astonishment of the physicians and friends what was the trouble; or the accidental expectoration of the foreign body established the diagnosis." Hoffmann believes that the stenotic form of bronchiectasis is of frequent occurrence, being present in many cases in which it is not recognized. Chevalier Jackson urges the importance of considering each case of bronchiectasis as a possible foreign body one. "Of course, it is not known how frequently foreign bodies may be the cause of the bronchiectasis, but the similarity of the symptoms in bronchiectasis and in foreign bodies in the bronchi would certainly render exploratory bronchoscopy advisable even in a case with negative radiograph." The importance of this warning has recently come home to me as the following case report will testify.

CASE II.—Foreign body; bronchial stenosis; bronchiectasis. W. D., aged seven years; schoolboy. Referred by Dr. Mighell, Marshalltown, Iowa. September 25, 1911. Clinical No. 336. Complaints: "Cough and vomiting."

Family History. The family history was negative for tuberculosis.

¹⁷ Abhandl. d. Schles. Gesselsch. f. Vaterl. Kult. Phil. Hist. Abth. (Breslau), 1862, Heft i, 72.

Personal History. At the age of three he had lobar pneumonia, at five pertussis, and at six measles. Since the latter the patient had never been quite well.

Present illness began in February, 1911, with a severe cough occurring in paroxysms and associated with "vomiting up" of large amounts of yellow very offensive sputum. This might occur at any time during the day upon exertion or crying, but was more frequent and most abundant in the early morning. It was at times blood-streaked. The mother had noticed that the fingers were becoming short and stubby and that he was losing weight. A diagnosis of pulmonary tuberculosis was made by various physicians, and the sputum was examined repeatedly for tubercle bacilli, but with negative results. He first reported to the University Hospital in August, 1911, when he was examined by my associate, Dr. Van Epps, and a diagnosis of bronchiectasis made.

Physical examination on September 25 revealed a rather poorly nourished undersized boy weighing forty-one pounds. Face was pale. Definite clubbing of the terminal phalanges of both hands. The thorax was well-formed and symmetrical, but the right side moved less freely than the left. There was an area of definite dullness in the lower right back extending from the sixth dorsal spine to the base and from the posterior axillary fold to the spine. Over this area the breath sounds were amphoric and accompanied by numerous coarse moist rales. The left lung was clear on percussion, but revealed a few fine moist rales over the lower back. The heart showed no evidence of displacement or hypertrophy and the sounds were clear and of relative normal intensity. The pulse was 120, regular in force and rhythm, and of moderate volume. The abdomen was negative. On a subsequent examination, the breath sounds over the dull area were suppressed, and it was noticed that these varied with the recentness of the paroxysm of the cough and expectoration. Hemoglobin, 60 per cent. (Sahli); red cells, 4,400,000, white cells, 21,000. The sputum was excessive, varying from 100 to 300 c.c. in the twenty-four hours; it was purulent, greenish in color, and settled into the characteristic three layers, and had an offensive odor. Microscopically on numerous examinations there were neither elastic tissue nor acid-fast bacilli, but great numbers of pus cells and diplococci, and occasionally some blood cells. A skiagram (Fig. 2) revealed a dense shadow corresponding to the dull area at the right base and merging with the right border of the heart.

He was given daily intratracheal injections of iodoform, with gradual amelioration in the amount of sputum and in the severity of the cough. During the last week of his stay in the hospital the amount varied between 20 and 140 c.c. in the twenty-four hours. As a precautionary measure, a day or two before discharge, an aspirating needle was introduced into the right pleura and into

the right lung, but no pus could be obtained. He was discharged on November 18, 1911, having gained six pounds in weight, and looking and feeling much better.

On December 12, 1912, Dr. R. F. French, of Marshalltown, Iowa, reported that the patient, during a fit of coughing, had brought up a tack which he remembered having swallowed in June, 1910, but which neither mother nor patient had thought of from that time. Upon receipt of this letter we immediately reexamined the skiagram and found that we had overlooked the definite shadow of the tack lying head downward in one of the large bronchi of the right side. Dr. G. E. Hermence, who subsequently had charge of the patient, elicited the following new facts from the

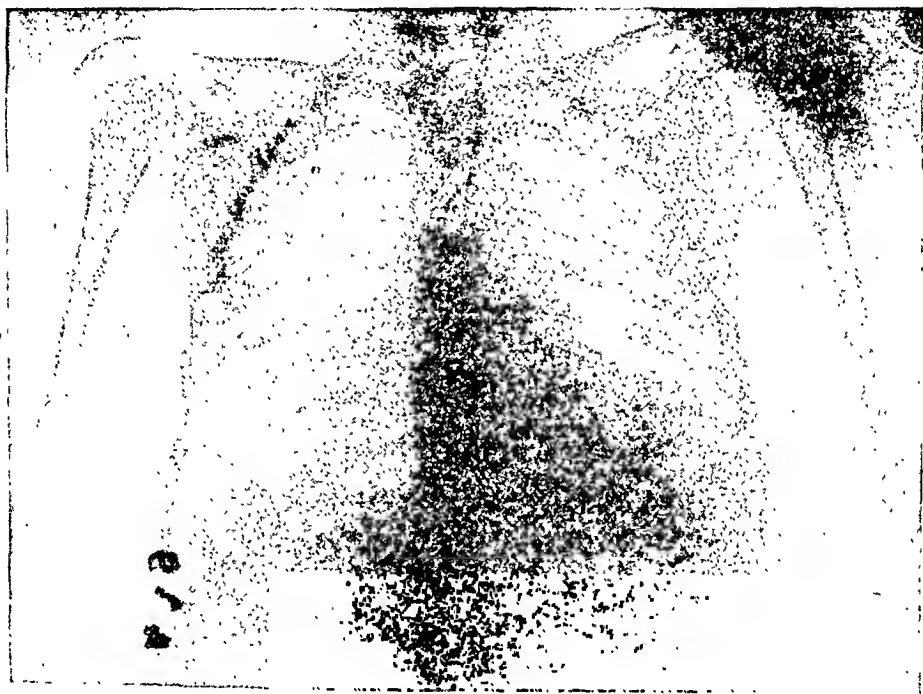


FIG. 2.—Case II. Foreign body; stenosis; bronchiectasis.

mother: She now remembered that the boy had swallowed the tack in June, 1910. At the time he had had a hard coughing spell, but recovered and the tack was forgotten. In January, 1911, he began to cough, especially in the morning, and it was noticed that he raised a large amount of sputum and had distinct fever, as high as 104° on one occasion. Since his discharge from the University Hospital the intratracheal injections were continued until September, 1912, when they were stopped on account of local irritation of the throat. About September 1, he was worse again, and in one of the paroxysms something seemed to "break in his side," which was followed by an unusually large amount of yellowish purulent material. In another violent paroxysm, on December 3,

something seemed to choke him, and upon putting his finger into the pharynx he pulled out the tack (Fig. 3). Since then the patient has felt better. The cough and sputum have gradually become less. A request for him to return to the hospital for examination was not granted, but Dr. Hermence, under date of April 24, 1913, reported that the cough and sputum have much lessened and that the latter has little or no odor. He had gained in weight, and now leads the normal life of a boy of his age. The physical examination still reveals an area of dulness at the original site.

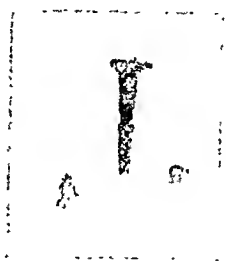


FIG. 3.—Tack expelled from bronchus by Case II. Note slight erosion of the head of shaft.

Hoffmann calls attention to the probable frequent origin of bronchiectasis from inhalation of solid particles. It is of interest to note that Case I of our series assigned the recent exacerbation of the cough and expectoration to the inhalation of coal particles while working in a railroad coal chute.

The importance of bronchial stenosis in the etiology of bronchiectasis has been demonstrated experimentally by W. G. MacCallum¹⁸ and his pupils W. L. Thorton and J. P. Pratt.¹⁹ Bronchial stenosis was produced either by a screw clamp around a bronchus or by placing short pieces of tubes, with different sized lumens, inside of the bronchus. When one bronchus was partially occluded the pressure changes in the lung behind the occlusion were marked; the greater the occlusion the greater the negative pressure on inspiration, and the greater the positive pressure on expiration. In addition, inspiration and expiration were so protracted that the opportunity for a pause no longer existed, and they occupied the whole cycle. When the lumen of a bronchus was reduced the lung corresponding to the bronchus involved failed to contract during expiration as completely as the lung with an unobstructed bronchus. Owing to this failure to completely contract an excess of air remained in the lung, which was consequently continually distended. What has been represented in these experiments as taking place rapidly must appear gradually in man as the result of a bronchial stenosis, due to the pressure of a tumor or some similar cause. If a foreign body be lodged in a bronchus the above changes

¹⁸ Bull. Johns Hopkins Hospital, 1908, xix, 215.

¹⁹ Ibid., 1908, xix, 230

must follow very rapidly. "The partial occlusion of a bronchus causes air to be entrapped and the bronchus to be distended, with greater changes in pressure behind the obstruction during respiration. In coughing and related processes the pressure inside the bronchus is greater than the pressure outside the bronchus only by the force of the elastic recoil of the lung; so there is no marked tendency on the part of the bronchi to undergo dilatation."

3. *Bronchial Obstruction.* According to Lichtheim²⁰ sudden and complete obstruction of a bronchus causes in twenty-four hours collapse of the lung area to which it is distributed with purulent accumulation within the tubes. This is followed by emphysema of the surrounding tissue and in several weeks by dilatation of the neighboring bronchus. Occlusion of the bronchus does not necessarily cause a bronchiectasis in the area of supply unless there is also an opportunity for the development of a purulent bronchitis; hence a stenosis is more favorable for its development than an absolute occlusion. This was well illustrated in a case reported by Sutherland,²¹ in which the bronchial obstruction was due to the impaction of an O'Dwyer tube; at the autopsy the greater part of the lower lobe was destroyed by an abscess and the remaining portion was collapsed and airless; the surrounding smaller bronchi were dilated and embedded in soft friable lung tissue.

B. *Extrinsic*, that is, conditions acting indirectly through disease of the lungs or pleuræ.

1. *Pulmonary Changes.* (a) *Collapse of the Lung.* This exciting cause is common in the child as a result of capillary bronchitis or of bronchial stenosis, as has already been described.

(b) *Pneumonia.* Either the lobar or lobular variety is regarded by many as a common cause. It must be borne in mind that lobular pneumonia also frequently supervenes in a well-established bronchiectasis. (Compare Case III.)

(c) *Emphysema.* A moderate degree of bronchiectasis is usually found associated with old-standing cases of emphysema.

(d) *Fibrosis of the Lung.* Fibrosis of the lung, sometimes termed cirrhosis of the lung, may result from an unresolved or chronic pneumonia or from the fibrosis developing in certain cases of pulmonary tuberculosis. Ewart emphatically states that bronchiectasis (Rokitansky to the contrary) may occur in subjects of chronic phthisis; on the other hand, chronic bronchiectasis may end in tuberculosis, though this is a rare event.

Hoffmann believes a tuberculosis establishing itself in the finer branches of the bronchi may lead to the formation of small bronchiectatic areas, which, however, do not produce clinical symptoms and are therefore not named in the clinical account of bronchi-

²⁰ Archiv f. experimentelle Pathologie u. Pharmakologie, 1879, x, 54.

²¹ Lancet, 1892, i, 189.

ectasis. In many cases of so-called fibrous phthisis characteristic bronchiectasis occurs, and their course will indicate that the cicatricial contraction of the tissue was really the cause of the bronchial dilatation.

Syphilis in the form of bronchial gummas has already been referred to, but it must be mentioned that specific scar formation and infiltration of the parenchyma are especially favorable for the production of bronchiectasis.

2. *Pleural Changes.* Pleurisy with effusion, whether serous or purulent, will result in collapse of the lung; dilatation of the bronchi and chronic thickening of the interlobular and interalveolar connective-tissue may follow in the order named, or these changes may proceed together. Extensive pleuritic thickening at the base cripples the lung and the respiratory function may be entirely lost.

In a given case it is difficult if not impossible to state which one of these various extrinsic factors is responsible for the bronchiectasis. In fact they may all be present in any one case, and it is perhaps best to group those cases under the general term of "pleuropneumonic." The following histories are illustrative:

CASE III.—Pleuropneumonic bronchiectasis. A. C., aged fourteen years; schoolgirl; white; American. Clinical No. 405. Admitted September 17, 1910. Referred by Dr. Post of Maquoketa. Complaints: "Cough and profuse expectoration."

Family History. Negative for tuberculosis or other lung trouble.

Personal History. Had chickenpox and measles in early childhood. In 1903 she received an injury (?) to the back, from which she was confined to bed on account of pain, cough, and high fever.

Present illness began in December, 1907, with an attack of scarlet fever, complicated by severe pain in the left side. It was not known whether the patient had a pneumonia or a pleurisy at that time. For two years subsequently she suffered from a troublesome cough, but without sputum. About September, 1909, expectoration made its appearance. It was profuse, yellowish in color, and with an offensive odor, and at times blood-streaked. The cough became paroxysmal, occurring at intervals during the day, but more particularly in the morning. She averaged about five or six attacks in the twenty-four hours. She did not notice any effect of posture. At times the sputum would fill a teacup. During the last two or three years the mother had noticed gradual enlargement of the finger tips, and a liability to chills, fever, and sweating. The patient had lost ten to twelve pounds in weight. There had been slight cyanosis.

Physical examination showed that the patient was still well-developed and nourished. Weight, eighty-four pounds. The finger tips were markedly clubbed and the nails incurved; there was also slight clubbing of the big toes, with incurvature of the nails, but no enlargement of the bones. The thorax was decidedly long and

narrow, with a somewhat acute costal angle. The left upper front was flatter and moved less with respiration. The right lung was resonant, and except for somewhat harsh breath sounds in the second and third right interspaces and a few medium moist rales over the back, was normal throughout. The left lung revealed an area of dullness beginning at the level of the fourth dorsal spine and extending to the base and outward to the midscapular line. Over



FIG. 4.—Case III. Pleuropneumonic bronchiectasis.

this dull area the breath sounds were enfeebled, except after a paroxysm of coughing, when they became distinctly bronchial, and almost amphoric in character. Everywhere throughout the left lung, but particularly over the lower lobe, were heard numerous medium and large moist rales. There was no displacement of the heart, no evident enlargement of the right chamber, and no abnormality of the heart sounds. The sputum varied in amount from 410 to 200 c.c. in the twenty-four hours. It presented the charac-

teristic three layers, had a greenish-yellow color and a fetid, sweetish odor. It contained many pus cells, but daily examination failed to show the presence of elastic tissue or tubercle bacilli. The blood count on September 22 revealed hemoglobin, 80 per cent. (Tallquist); red blood cells, 5,060,000; white blood cells, 12,000. Differential count: Polynuclears, 75 per cent.; lymphocytes, 14 per cent.; large mononuclears, 10 per cent.; eosinophiles, 1 per cent. The von Pirquet test was negative on two occasions. The skiagram (Fig. 4) on September 17 revealed enlarged glands in the hilum of the right lung. On the left side below the cardiac shadow there was an abnormal opacity, 10 cm. in diameter, corresponding in position to the signs of the cavity on physical examination. On September 27 she was started on the intratracheal injections of iodoform. In addition she received general dietetic and hygienic supervision. With the exception of a sudden onset of chill, fever, pain in the left side, and the presence of a dry friction rub, due to an infection of the left pleura on October 24, 1910, and again on January 17, February 25, and February 28, 1911, the patient gradually and progressively gained in strength and weight, and the amount of sputum fell to about 75 to 100 c.c. in the twenty-four hours. On February 28 the patient coughed up 270 c.c. of fetid sputum, which suggested a temporary obstruction to the outflow of the cavity, though on this as on previous occasions a friction rub was audible. On March 14, 1911, the white blood cells were 8000, and the polynuclears 88 per cent. On March 21 the patient was discharged, having gained twenty-four pounds in weight, and having only one or two paroxysms in the twenty-four hours. The sputum on the last day measured 60 c.c. The signs at the left base, however, remained unaltered. In the hope of finding a definite abscess cavity and draining the same by surgical means, an aspirating needle was introduced into the ninth interspace in the back corresponding to the middle of the dull area, but no pus could be obtained.

A letter from the mother on March 25, 1913, reported that the patient weighed 125 pounds, which meant an additional gain of fourteen pounds since discharge. The cough and sputum, however, persisted.

CASE IV.—Pleuropneumonic bronchiectasis. C. M., male, aged seventeen years; schoolboy. Referred by Dr. W. H. Spencer, of Cedar Rapids. Admitted October 27, 1910. Clinical No. 83. Complaints: "Stomach trouble." Father and mother, four brothers, and three sisters living and well. Tuberculosis on both paternal and maternal sides of family.

Personal History. Patient was born and bred in Iowa. He had measles and whooping cough in childhood, but denied pneumonia and pleurisy previous to the present illness. The mother stated that he had been subject to winter cough since his eleventh or

twelfth year, associated with sputum. Average weight at fifteen years was 115 pounds.

The present illness dated from his fourteenth year, when he had an "abscess in the left side," since which he had never been strong. For the last three years he had practically a constant cough, associated with the expectoration of large amounts of greenish-yellow and offensive sputum, especially profuse in the early morning. At fifteen years he had several attacks of hemoptysis. He had dyspnea on exertion and fever until six months before admission. The appetite became poor, and he had lost steadily in weight. The sputum had been repeatedly examined for tubercle bacilli, but with negative results.

Physical examination revealed a tall, slim, delicate-looking youth of blond complexion. Weight, 107 pounds. There was dyspnea on the slight exertion of undressing. He was a mouth breather. There was definite clubbing of the finger tips and well-marked incurvature of the nails, with slight cyanosis of the nail beds. The thorax was large, well-developed, and slightly asymmetrical in front, the left side being smaller than the right and expanding less. The left back seemed flatter than the right. The percussion note was everywhere resonant except in the lower left back, where it was impaired, though not actually dull. Over the impaired area tactile fremitus and vocal resonance were somewhat increased, while the breath sounds had a distant blowing, almost tubular quality. Over the entire left back there were numerous medium moist rales, with here and there a fine crepitant rale. The right lung was resonant throughout, while the breath sounds were vesicular except in the lower right axilla and right back from the angle of the scapula to the base, where they were distinctly harsh and accompanied by numerous medium moist rales and bronchophony. The heart was neither hypertrophied nor displaced. The heart sounds were clear at the apex, while at the base the pulmonic second sound was distinctly accentuated. The pulse varied from 90 to 112 to the minute, regular, of fair volume, and moderate tension. The abdomen was flat and soft, and neither liver nor spleen was palpable. The blood revealed hemoglobin, 53 per cent. (Sahli); red blood cells, 5,250,000; white blood cells, 15,600. Differential count: Polynuclears, 73 per cent.; lymphocytes, 24 per cent.; large mononuclears, 3 per cent. The urine was normal. The sputum varied in amount from 150 to 190 c.c. in the twenty-four hours, and had a distinctly sweetish odor at times, but at others was offensive. Microscopically it was negative for acid-fast bacilli and elastic tissue on seven observations. The von Pirquet test proved negative. Temperature ranged between $98\frac{1}{2}^{\circ}$ and $99\frac{4}{5}^{\circ}$. On October 27, 1910, a skiagram (Fig. 5) revealed a distinct shadow at the left base, merging with the heart dulness. There was also a slight increase in the normal shadow at the right hilum and a little opacity at

the right base. The patient received a few intratracheal injections, after which he went home with directions to his physician to continue treatment. He was lost sight of, and a letter from Dr. Spencer on April 14, 1913, reported that he had died some two years after his discharge from the hospital.

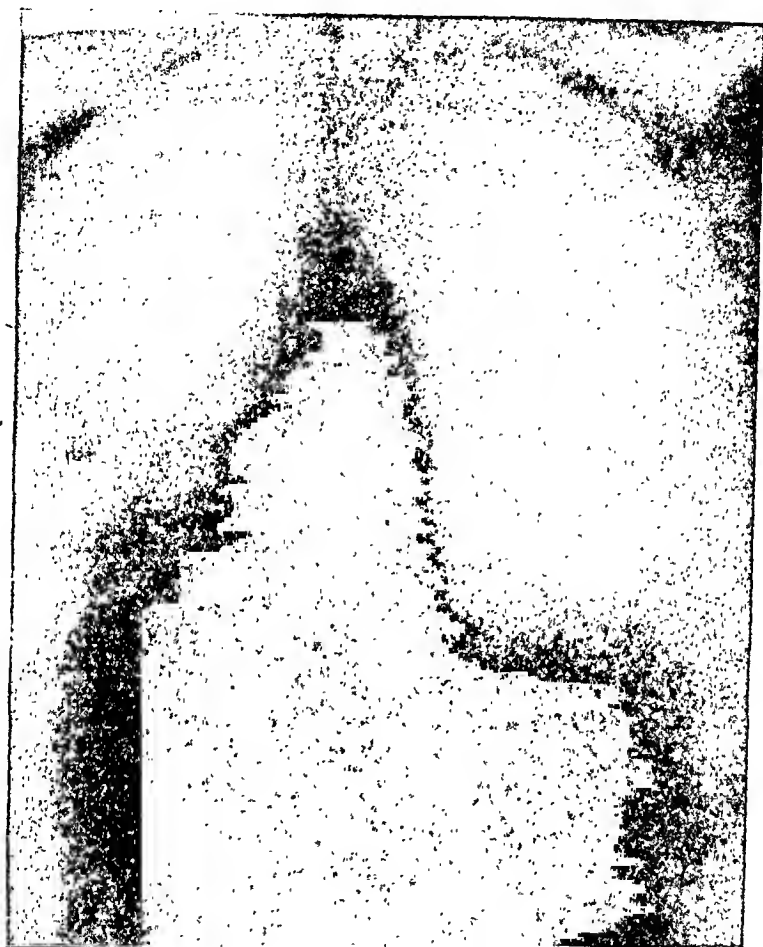


FIG. 5.—Case IV. Pleuropneumonic bronchiectasis.

PATHOGENESIS. The best *resume* of the various theories of the production of bronchiectasis is given by T. Grainger Stewart and G. A. Gibson,²² and will be adopted in this paper with some modifications and additions.

1. The mechanical pressure of the stagnating secretion was first suggested by Laennec and adopted by other French pathologists. According to this theory the accumulation of the mucus, aided to a certain extent by cough, causes the dilatation. But there is no special accumulation of mucus in some cases, and further,

²² Twentieth Century Practice of Medicine, 1896, vi, 552 (New York, Wm. Wood & Co.).

it is mechanically impossible when one considers the consistency of the secretion and the free outlet in two directions.

2. Concentrated air pressure is advocated by Reynaud, Williams, and others. The dilatation is explained as compensatory to atrophy or collapse of neighboring areas of the lung. Further, the pressure of the inspired air acts with greater force on the diminished respiratory surface. Against this theory are two facts: (1) Bronchiectasis arises without preëxisting cough, and cough is common while bronchiectasis is rare; (2) even if such a cause were present, emphysema rather than bronchial dilatation would result, for the bronchi are less yielding than the pulmonary tissue.

3. Extrabronchial traction was emphasized by Corrigan, Barth, and Hamilton. According to them dilatation resulted from traction upon the bronchial walls by the contracting cirrhus lung tissue aided by pleuritic adhesions to the chest wall. Against this speak the following facts: (a) Bronchiectasis often occurs without cirrhosis and without pleural adhesions; (b) the possibility to demonstrate that the dilatation may precede in some cases the condensation of the lung; (c) the process of traction could never explain the opening of the dilatations into one another nor the formation of bridges in the dilated portions; (d) cirrhosis of the lung does occur without bronchiectasis, the latter being present in only 30 per cent. of the former according to Bastian.

4. Inflammation of the bronchial wall was first advanced by Stokes and adopted by Wilson Fox among others. They pointed out that the bronchial wall, as the result of the inflammation, loses its elasticity, contractility, and ciliary movement; the bronchi consequently dilate, and so an accumulation of secretion occurs. Yet if bronchitis leads to bronchiectasis, why is the former so common and the latter so rare? McPhedran²³ answers this by saying that "inflammation of the bronchi to be effective in causing dilatation must be destructive; it must destroy the structure which gives resisting power to the bronchial wall, namely, muscular tissue, elastic tissue, and cartilage." Another objection, however, is that bronchiectasis may develop without preëxisting bronchitis; and lastly, the walls of the dilatation are not infrequently found atrophied and without signs of inflammation.

5. Nervous theory: Lebert thought the loss of power of the bronchial walls was dependent rather more upon nervous influences than upon inflammation. Stewart and Gibson regard this theory as purely hypothetical and gratuitous, and point out that in analogous processes as aneurysm, varicose veins, and staphyloma posticum there is no reason to look for nervous causes but rather local nutritional changes.

²³ Osler's System of Medicine, Oxford, 1908, iii, 681.

6. Primary atrophy of the bronchial wall: This explanation of the origin of bronchiectasis was first advanced by Grainger Stewart in 1867, founded upon a series of pathological and clinical observations. In Stewart's opinion it offered a satisfactory explanation of the most important and commonest groups of cases which he terms primary, while he fully admits the existence of other secondary varieties. "The process then is to be regarded as analogous to the direct atrophic form of emphysema and not improbably to result from a constitutional possibly an hereditary effect."²⁴ In primary bronchiectasis the essential element is an atrophy of the bronchial walls; the cause for such atrophy is not yet understood, but it is probably connected with constitutional peculiarities. The walls of the bronchi being so thinned and weakened, yield to the ordinary air pressure, or it may be that deep and sudden inspiration or violent muscular exercise or the sudden expiratory efforts made while the glottis is closed in the act of coughing aid in the process of dilatation. The existence of dilatation favors the accumulation of mucus, and this in turn to inflammation and formation of villous processes, increased connective tissue, irritation of the cartilages, and to consolidation of the surrounding lung and pleuritic adhesions.

The secondary bronchiectasis may occur in the course of various morbid conditions of the surrounding lung tissue or be due to mechanical obstruction to the free passage of air in inspiration and expiration. The explanations of the pathogenesis of bronchiectasis advanced by most writers apply to these secondary cases: "How much influence to assign to each of these causes in any given case is difficult to determine."

7. Ewart's explanation: William Ewart²⁵ has pointed out that the common feature of all cases of bronchiectasis is faulty distribution of space between the air tubes and pulmonary tissue. Any excessive stress ultimately finds out the least resistant tissue, which is most often the pulmonary, and therefore becomes emphysematous; if, however, the bronchi are previously diseased they may suffer. In disease, therefore, other mechanical factors arise, namely: (1) Within the bronchi an accumulation of mucus and an antecedent or resulting degeneration of the bronchial wall; (2) changes induced in the lung tissue may bring about a faulty allotment in space, namely, (a) emphysema, much of which is effect, not cause; (b) collapse, which when occurring unevenly at one side of a bronchial tube may act as one of the agents of dilatation; (c) increase in the subpleural, perilobular, and interlobular stroma.

"As to the general mechanism of the dilatation we must again look for some elementary factor common to all varieties, and this we find in obstruction in the broadest sense of the word." Owing to the alternating direction of air currents an obstruction may lead

²⁴ Stewart and Gibson, loc. cit.

²⁵ Loc. cit.

to dilatation either on its proximal or on its distal side. The dilating force is usually not as in other tubes, as the alimentary tract, due to the pressure of an internal accumulation, but has its seat on the distal side of the dilatation; it is an aspirating not a forcing pressure. "The inspiratory traction made by the chest wall if it should fail to expand an obstructed lobule, might be transmitted to the delicate air tube adjoining the latter and might dilate it. Owing to the solidarity existing between all parts of the lung, this encroachment of bronchial space into the vacated pulmonary space may occur at a distance from the original collapse." The progressive increase in the dilatation may be brought about according to either the inspiratory or the expiratory hypothesis. In the former, according to Laennec, an abnormal inspiratory effort preceding cough throws a damaging stress upon the weakened parietes of the bronchial tube. The expiratory hypothesis has been advanced for bronchiectasis as for emphysema. In expiration with the glottis closed the pressure may rise to 80 mm. of mercury and in severe coughing to 110 mm. or more, while in quiet expiration it does not exceed 2 or 3 mm. During inspiration the air is sucked through the stenosis but in expiration the expelling force is often insufficient, for the expelling force in this case is represented only by the elasticity of the tissue lying beyond the constriction. If a mass of mucus is present it may act like a valve, so that air can get in much more easily than it can get out. Stagnation of the air results, the pressure becomes very high and remains so continuously. This is greatly assisted by attacks of coughing. Yet if we accept this we must answer the question why it is that bronchiectasis and emphysema are not universal inasmuch as we are daily subjecting our bronchial tree to an intense muscular strain with closed glottis. Evidently this immunity is dependent upon a perfect distribution of pressure in the healthy lung. Cough may be powerless to dislodge the secretion and yet propel it far enough to cut off the dilated alveolus from the main bronchus. The result of a recurring valvular obstruction of this kind would be not only continued fulness of the dilatation while the surrounding tissues are being relieved of much of their air, but a maintenance within it of the highest air pressure at the time when the air pressure in its vicinity is at its minimum. Hoping to obtain some light on this theory, I turned to the studies of Tendeloo on *Emphysema*.²⁶ In this I was disappointed, as there was nothing in these technical papers on the dynamics and statics of emphysema that I could find in any way applicable to the mechanism of bronchiectasis.

Ewart shows how cough, bronchial catarrh, interstitial pneumonia, pleuropneumonic fibrosis, and stenosis may each and all

²⁶ Studien über die Ursachen der Lungenkrankheiten, 1902 (Wiesbaden, Bergmann); *ibid.* Ergeb. d. inner. med. u. Kinderheilk, 1910, vi, 1.

bring about an abnormal distribution of air space between the tubes and pulmonary tissue. It must be confessed that after due consideration of the various theories advanced it would seem that Ewart's hypothesis is the broadest and the most logical.

CONCLUSIONS. 1. Bronchiectasis is a not infrequent clinical condition, and is too often mistaken for pulmonary tuberculosis.

2. The possibility of a foreign body or syphilitic stenosis must always be excluded as etiological factors.

3. Skiagrams are helpful in the case of a foreign body, but bronchoscopy should be carried out to exclude a foreign body and to treat a possible stenosis of a bronchus.

4. The etiology is manifold, but the inflammatory causes are the most common.

5. Of the various theories that advanced by William Ewart is the most rational and scientific. It considers a faulty distribution of air space as a predisposing factor common to all cases. The general mechanism of dilatation is found in obstruction in the broadest sense of the word.

SPONTANEOUS RUPTURE OF THE SPLEEN IN TYPHOID FEVER, WITH REPORT OF A CASE CURED BY OPERATION (SPLENECTOMY).

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THE spontaneous rupture of the spleen in the course of typhoid fever is sufficiently rare to warrant the report of a case, more especially as in this instance it was possible to make the diagnosis and, by prompt operation, to save the life of the patient. Only 12 other cases are recorded in the literature. In 9 of these the condition was discovered at autopsy. In the 3 remaining cases it was found in the course of operation done for supposed intestinal perforation. None of these cases recovered.

A physician, aged thirty-six years, was admitted to the New York Hospital on February 20, 1913, with the diagnosis of probable typhoid fever. Up to the onset of his symptoms, seven days before, he had never been seriously ill in his life. He had never had malarial fever nor any other disease likely to lead to enlargement of the spleen. At the onset the symptoms were those of a catarrhal cold,

sore throat, and slight cough. With these were increasing fever, headache, general body pains, malaise, weakness, and troublesome nausea.

Physical Examination. Muscular, well-nourished body. High color and flushed face. Moist, slightly coated tongue. Throat somewhat congested. Chest well-developed. Lungs show everywhere normal resonance. Good vesicular, respiratory murmur. No adventitious sounds, except an occasional sonorous rhonchus. Heart normal in size and position. Apex-beat felt in fifth space, 8 cm. to left of the midsternal line. Sounds clear and normal in character. Action regular and strong. Pulse large, full, and slightly rapid. Palpable arteries normal. Abdomen full and soft. No rose spots. Liver dulness extends in mamillary line from the sixth rib to the free border. Liver edge not felt. Both kidneys indistinctly felt; not tender. Area of splenic dulness is considerably increased and extends from the eighth to the eleventh rib and anteriorly 3 cm. beyond the costal margin. The edge of the spleen is distinctly felt, even with quiet respiration. On deep inspiration it extends fully 4 cm. below the costal margin. It is unusually broad; its edge is blunt and rounded and its consistence noticeably firm and tense. Palpation of the spleen causes distinct tenderness. The extremities are normal. There is no enlargement of the superficial lymph nodes. On admission temperature was 100.4°; respirations, 22; pulse, 88.

February 21. The patient passed a restless night, with much headache and general discomfort, and these symptoms continued throughout most of the day. At 7.15 p.m. he complained of a sudden, sharp, stabbing pain in the left hypochondrium. This was soon followed by severe aching pain in the left shoulder, which radiated somewhat down the left arm. Soon after the onset of the pain he vomited a small quantity of clear fluid and broke into a profuse perspiration. The pain was so severe as to require an injection of morphine. The respirations were rapid and shallow; there was marked tenderness to pressure just below the costal margin, where the spleen could be distinctly felt, and slight rigidity of the upper part of the left rectus muscle. At times the pain was felt somewhat in the right hypochondrium.

February 22. The severe pain in the left side and left shoulder continued throughout the night, in spite of a second injection of morphine. When seen in the morning the patient looked much more seriously ill. His eyes were sunken, his features drawn and anxious, his respirations shallow and hurried. There was still distinct tenderness in the left hypochondrium and slight muscular rigidity, so that the spleen could not be felt distinctly. The area of splenic dulness, however, seemed larger than on admission. Elsewhere the abdomen was soft and showed no tenderness on palpation. At the base of the left chest posteriorly the respiratory

murmur was feeble, and a distinct friction sound could be heard both on inspiration and expiration. The spontaneous pain had lessened, but was aggravated by the slight dry cough that was present. The ache in the left shoulder and left supraclavicular fossa persisted.

February 23. The patient passed a restless, uncomfortable night, complaining chiefly of headache and nausea. At times he was slightly delirious. During the day his general condition and appearance improved much, and he was able to take and retain a fair amount of liquid food. The bowels were moved satisfactorily by an enema. The pain in the left side had ceased to be troublesome, but there was still slight tenderness in the left upper quadrant. The physical signs in the chest were unchanged, and it was still impossible to determine the nature of the violent attack he had had two days before. The occurrence of a pulmonary infarct was suspected, but neither the symptoms nor the physical signs were sufficiently characteristic to justify that diagnosis. The extremities showed no indications of thrombophlebitis.

February 24. The patient's general condition had still further improved and he passed a comfortable day and night and seemed to be settling down to a fairly normal typhoid course. Although the Widal test was still negative, blood cultures taken on February 21 showed a Gram-negative bacillus which resembled the *Bacillus typhosus*, and which two days later was identified positively as such.

On the morning of February 25 the patient awoke refreshed after a comfortable night. At 8.30 A.M., however, he had an attack of coughing and immediately afterward complained of the same severe pain in the left hypochondrium and left shoulder. This pain continued throughout the morning, and was accompanied by profuse sweating and by the same startling change in appearance and general condition. When seen by one of us (Conner) about 11.30 A.M., he had, in even more marked degree, the sunken eyes, the pinched features, and anxious look that had characterized his first attack. His pulse was rapid, small, and soft; his respirations also were rapid, the skin was covered with cold sweat, and he complained of weakness and nausea. It was evident that something serious had happened, and that his condition was growing progressively and rapidly worse. Examination of the chest showed no change from that of the preceding days. Aside from some diminution of the respiratory murmur at the left base posteriorly and a few rales the pulmonary signs were normal. There was dulness on percussion over the greater part of the left side of the abdomen and in the left flank, and some rigidity and tenderness in the left upper quadrant. The rest of the abdomen was soft and while having a somewhat boggy feel, was not tender. The liver dulness was normal. Drs. William A. Downes and S. W.

Lambert were called in consultation, and it was agreed by all of us that the symptoms indicated a rupture of the spleen. This diagnosis was arrived at by considering the location of the pain, tenderness, and muscular rigidity; by the absence of signs pointing toward other likely complications, such as intestinal perforation and pulmonary infarction, and by the fact that the spleen had been recognized as being unusually large and tense for the early days of typhoid fever. With the hope of obtaining some confirmation of severe hemorrhage a blood examination was made about three and a half hours after the onset of the pain, and when the symptoms pointed strongly to an alarming loss of blood. The examination gave the following results: Red cells, 5,280,000; hemoglobin (Sahli), 85 per cent.; leukocytes, 35,000.

In spite of these apparently inconsistent blood-findings an immediate exploratory operation was decided upon, and at 1.45 P.M. (five and a quarter hours after the onset of the symptoms) the patient was taken to the operating room. The temperature, which at 8 A.M. had been 102.8°, was 100°, respirations 32, pulse 118. Dr. Downes, under local anesthesia, opened the abdomen by a vertical incision through the middle of the left rectus muscle. Upon opening the peritoneum the abdomen was seen to contain a large amount of blood. The patient was therefore given nitrous oxide gas and ether (by Dr. Thomas L. Bennett) and the incision was rapidly enlarged to an extent of eight inches. A tremendous quantity of fresh and clotted blood, estimated at from one and a half to two quarts, escaped from the abdomen. The left hand was passed immediately to the pedicle of the spleen which was grasped between the index and middle fingers, and the spleen delivered through the wound with the right hand. At this point the pedicle was caught with a long, straight, rubber-covered clamp placed close to the spleen. The vessels were then ligated, about two inches proximal to the clamp, with No. 2 chromicized catgut. The larger blood-clots were rapidly removed; one old and laminated clot, fully an inch thick, conforming to the size and shape of the phrenic surface of the spleen, was found high up under the diaphragm. The abdomen was closed by layer sutures without drainage. Time of operation, twenty minutes.

When the hand was first passed behind the spleen, lying in its bed, a rent in the capsule, fully three inches in length, was encountered, running along the posterior border, and during the manipulation this rent was so enlarged by the time the organ was brought out of the wound that the capsule had been stripped from almost half its surface.

In spite of his critical condition on the operating table, which required an intravenous infusion of salt solution, the patient improved steadily during the succeeding twelve hours. His loss of fluid was replaced by saline solution given by hypodermoclysis

and by the Murphy "drip." At 10 P.M. the hemoglobin percentage had fallen to 62 and his leukocytes numbered 68,000. On the following morning (February 26) the pulse had fallen to below 100 and his general condition was satisfactory. At 2 P.M. an examination of the blood gave the following results: Red cells, 2,810,000; hemoglobin, 58 per cent.; leukocytes, 36,400.

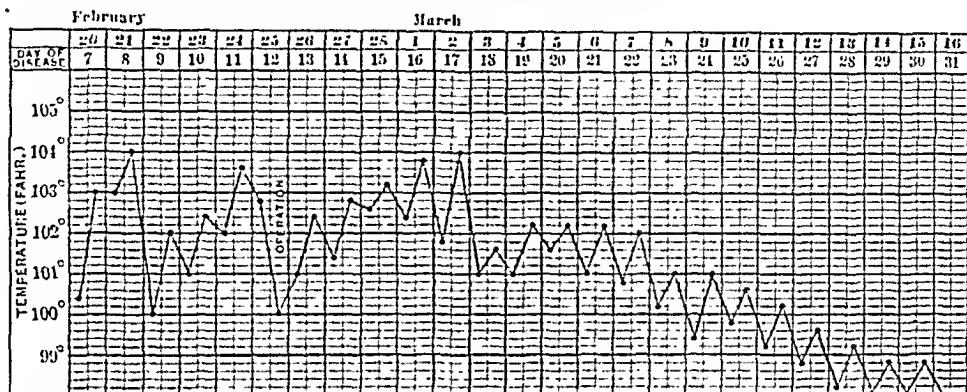


Chart of case of spontaneous rupture of the spleen in typhoid fever.

On March 2 the patient complained of some pain in the left shoulder. There was no cough or other symptoms, but examination of the left chest posteriorly revealed an area of dulness over the middle portion of the lower lobe and, corresponding to this, a small area over which bronchial breathing and bronchophony could be heard. At that time the extremities showed no signs of thrombophlebitis.

March 3. Widal test positive.

March 5. Slight tenderness on pressure over the lower part of the left calf. The median basilic vein of the right arm was thrombosed at a point distal to the place of the infusion puncture at the time of the operation, and showed as an indurated, tender cord 8 cm. long. The area of bronchial breathing in the left lower lobe had disappeared, but over the lower half of the lower lobe there was marked dulness, absence of breath sounds and fremitus, and distant nasal voice. There was slight cough and occasional pain in the left axilla, but no expectoration.

During the next few days the tenderness in the left calf became more pronounced and more extensive, and a similar area of tenderness appeared in the right calf, together with an indistinct elongated area of induration. These indications of thrombophlebitis gradually subsided, as did also the signs of pulmonary infarction.

By March 15 the temperature had reached normal and the patient was convalescent.

On March 31 he was able to leave the hospital, and one month later had regained his lost weight and seemed in almost his usual health.

TABLE OF BLOOD EXAMINATIONS.

Date.	Red cells.	Hemo- globin, per cent.	Leuko- cytes.	Polymorpho- nuclears.	Lymphocytes and large mononuclears.		
Feb. 20, 1913	8,800	71	17	11	
Feb. 22,	13,400	60	30	10	
Feb. 25, 12 M.	5,280,000	85	35,000	87	13		
Feb. 25, 10 P.M.	62	68,000	91	9		
Feb. 26, 2 P.M.	2,800,000	58	36,400	86	14		
Feb. 28	24,800	67	22	10	
Mar. 1	58	30,000	83	17		Normo- blasts. Myelo- cytes and normo- blasts Normo- blasts.
Mar. 12	62	15,800	82	17		
Mar. 23	71					

Pathological Report (Dr. Tytler). The spleen is of about normal shape, swollen, and firm, and measures 14 cm. in length by 11 cm. maximum width by 7 cm. maximum thickness. Weight, 375 grams. The anterior border shows one shallow notch near the anterior extremity. The capsule shows an extensive tear starting about the middle of the anterior border, following that border to the posterior extremity, thence obliquely across the renal surface to the middle of the posterior border, and thence along that border almost to the anterior extremity. The flap formed by this tear is loose and completely separated from the diaphragmatic surface. The capsule itself is thin, smooth, and transparent everywhere.

The separate mass of blood-clot received was removed from the diaphragmatic surface. It is disk-shaped and measures about 12 cm. in greatest diameter by 2 to 3 cm. in thickness. It is firm, dark reddish brown, and on section shows a definite laminated structure.

The surface of the spleen over the area from which the capsule was separated is smooth, dark red in color, and shows no laceration or rupture. On section the spleen cuts readily, leaving a swollen, congested, slightly indurated cut surface in which the lymph follicles and trabeculae can just be distinguished.

Microscopic sections show the spleen pulp much congested and packed with large phagocytic endothelial cells both in and between the sinuses. The endothelial lining of the sinuses is swollen and shows some proliferation. Small leukocytes are seen in the sinuses and between them. The pulp cords are compressed and the lymphocytes relatively fewer than natural. The lymph follicles are of about natural size and show no significant lesions. The whole picture corresponds to the usual findings in the spleen of typhoid fever.

The capsule in the section examined (from the hepatic surface) shows no abnormalities. It is of natural thickness, and consists of mature fibrous tissue, with no cellular infiltration.

DISCUSSION. The reasons for the diagnosis of rupture of the spleen have been given. The condition probably would not have been recognized had it not been for the fact that attention had been directed to the spleen by reason of its unusually large size and firm consistence. When once the possibility of its rupture had been thought of the symptoms seemed to correspond so perfectly with what might be expected under such circumstances that the diagnosis could be made without much hesitation.

Two further points of interest deserve mention. The discovery at operation of a layer of old, laminated clot lying directly over the dorsum of the spleen made it certain that the acute symptoms which appeared three days before the day of operation indicated the time of the first rupture of the splenic capsule. These symptoms had entirely subsided before the second attack of pain, which followed immediately upon an attack of coughing. At this time evidently there was either an increase in the rupture of the capsule or a displacement of the old clot and subsequent uncontrollable bleeding from the site of the old tear. The subsidence of the symptoms after the first attack of pain suggests the possibility that, rarely, a rupture of the capsule of the spleen may be followed by spontaneous cessation of the bleeding and recovery.

The second point of interest relates to the character of the blood, as shown by examination, at a time when all the symptoms indicated an alarming internal hemorrhage. At that time the red cells numbered over 5,000,000 to the centimeter and the hemoglobin percentage was 85. This apparent inconsistency was interpreted as meaning that the hemorrhage had occurred so rapidly that there had not been time for the circulating blood to take up any appreciable amount of fluid from the tissues, and that the blood in circulation, while greatly reduced in volume, was as yet unchanged in consistence. On the day after the operation the red-cell count was 2,800,000 and the hemoglobin was 58 per cent. It is interesting to note that although before the operation the red cells showed no material change in concentration, the circulating leukocytes had already increased to 35,000. That rapid, severe hemorrhage is followed by a rise in the number of leukocytes and in the percentage of polymorphonuclear cells is well recognized; but we have been able to find no mention of the fact, illustrated in the present case, that this increase in the leukocytes occurs much earlier than do the other characteristic blood changes—namely, the fall in the number of red cells and in the percentage of hemoglobin.

Spontaneous rupture of the acutely swollen spleen is a rare occurrence, but has been encountered in the course of various fevers. In tropical malarial fever it has been seen in a considerable number of cases. More rarely it has been observed in typhus, relapsing,

and typhoid fever. In the case of the last-named disease, Melchior¹ has been able recently to collect but twelve authentic instances of such spontaneous rupture.² Since his careful review of the subject no further cases have appeared in the literature. The rarity of this complication in typhoid fever may be further shown by the following statistics: Curschmann³ found two instances of it among 577 autopsies in cases of typhoid. Among 2000 typhoid autopsies in the Munich Pathological Institute it was observed 5 times (one of these was in a case of abscess of the spleen⁴). Among 474 fatal cases of typhoid observed in St. Jacob's Hospital, in Leipzig, between the years 1880 and 1907, no instance of rupture of the spleen was seen.⁵

Bryan,⁶ of Richmond, Va., has reported an interesting case of spontaneous rupture of the spleen in the course of typhoid fever, and has attempted to assemble all the reported cases; but in his collection of 28 cases he has included indiscriminately cases of ruptured spleen in typhus, relapsing, and malarial fever as well as in typhoid fever.

All of the 12 cases of spontaneous rupture in typhoid collected by Melchior occurred in males. Ten of those were adults, and 2 were boys, aged respectively eight and ten years.

As regards the time of the disease at which the rupture occurred, in 5 of the 13 cases (including our own) the signs of rupture appeared during or at the end of the second week; in 2 cases during the third week; in 1 at the end of the fifth week; in 1 during convalescence, and in 1 during an apparent relapse. In 3 cases there was no information upon this point.

The site of the rupture is mentioned in 7 of the 13 cases. In 3 instances this was in the region of the hilum; in 2 cases, near the lower pole; in 1 on the diaphragmatic surface, and in 1 (our own) along the posterior border. Usually the tear has been linear. In 1 case it was stellate; in 1 angular; in 1 it extended almost around the spleen near its middle. In most of the cases the tear has involved not only the capsule but the parenchyma as well. In our own case, however, and in that of Kammerer's, the tear was confined to the capsule; but in spite of this fact the hemorrhage in both cases was enormous.

¹ Die Spontanrupturen der Milz in Verlauf und Gelfolge des Typhus, abdominalis, *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, 1911, xiv, 810 and 897

² Melchior's collection includes thirteen cases, but one of these (Case 9) obviously cannot be regarded as an instance of spontaneous rupture.

³ *Der Unterleibstyphus*, Wien, 1893.

⁴ Holscher, *Ueber die Komplikationen bei 200 Fällen von letalem Abdominaltyphus*, Münch. med. Woch., 1891, p. 43.

⁵ Berg, *Statistik der im Krankenhaus St. Jakob in Leipzig in den Jahren, 1884-1893, behandelten Fälle von Typhus abdominalis*, Inaug. Diss., Leipzig, 1893. Piokowsky, *Statistik der im Krankenhaus St. Jakob in Leipzig während der Jahre 1893-1907, behandelte Fälle von Typhus abdominalis*, Inaug. Diss., Leipzig, 1907

⁶ Spontaneous Rupture of the Spleen in the Course of Typhoid Fever, *Ann. Surg.*, 1909, l. 857.

The duration of the symptoms in the cases of rupture of the spleen has varied from a few hours to two or three days. In Erichsen's case death is said to have occurred "in a few minutes." In 9 of the 12 cases collected by Melehior the condition was recognized only at autopsy. In the 3 remaining cases (Kammerer, West and Dudding, Bryan) the rupture of the spleen was discovered in the course of an operation done for supposed intestinal perforation. None of these cases recovered.

The *symptoms* of rupture of the spleen fall into two quite distinct groups: (1) the local symptoms of the rupture and of irritation of the neighboring peritoneum by the extravasated blood, and (2) the general symptoms of severe internal hemorrhage. In most of the cases described pain seems to have been the first symptom, although the location and character of the pain have usually not been given in much detail. In our own case there was severe pain referred to the splenic region, and also very severe pain in the left shoulder and in the left supraclavicular fossa. In West and Dudding's case the pain is said to have been referred to the central part of the abdomen. In addition to the pain there had usually been some tenderness and muscular rigidity in the left upper quadrant of the abdomen. In one of Chrostowski's cases the tenderness was extreme. The general symptoms, due to the progressive loss of blood, have been increasing collapse, pallor, rapid pulse, with falling temperature, restlessness, thirst, etc. In one case (Bryan) instead of a fall in temperature there was a rise to 106°.

The *diagnosis* of rupture of the spleen in the course of typhoid fever rests upon the association of the signs of local trouble in the left upper quadrant of the abdomen (pain, tenderness, muscular rigidity), with the evidences of progressive internal hemorrhage. In most cases the diagnosis ought not to be difficult if only the possibility of the occurrence of such a rupture is borne in mind. In our own case this possibility was suggested by the fact that the spleen had been recognized as being unusually large for the early days of typhoid fever. The difficulties of diagnosis will naturally be greatly increased in cases which are already gravely ill or in which delirium or great apathy mask the local symptoms. In the three earlier cases operated upon the condition suspected was that of intestinal perforation or perforation and hemorrhage.

Prognosis. Although all of the twelve previously reported cases have died, the evidence in our case that the first rupture occurred three days before the appearance of the symptoms which led to the operation, suggests the possibility that such a rupture may in rare instances be followed by spontaneous recovery. In general, it may be said, however, that the only chance of recovery lies in the prompt recognition of the condition and in immediate operation. In most instances the loss of blood has been so rapid and severe

that the delay of even a few hours would greatly imperil the chance of recovery, so that in any case in which there is a reasonable probability that the condition is one of rupture of the spleen the safest procedure would seem to be the making of a small exploratory incision under local anesthesia, as was done in the present case. If a rupture is found there seems to be no question that the prompt removal of the organ is greatly to be preferred to any attempt to check the bleeding by merely packing the wound in the spleen.

A summary of the twelve cases already reported is as follows:

CASE I.—Nüchel,⁷ 1839. A robust man, aged twenty-five years, was seized with diarrhea fourteen days before death. Two days before death he took to his bed with abdominal pain. Then followed collapse, pallor, sweating, cold extremities, and death.

Autopsy. Large, soft spleen, in the lower part of the outer surface of which was an angular tear three to four lines wide. Left hypochondrium filled with blood which extended throughout the left side of the abdomen as far as the true pelvis. There were numerous ulcers in the ileum.

CASE II.—Heimann,⁸ 1843. In an account of a typhoid epidemic in Moscow is a brief reference to a case in which the enlargement and softening of the spleen was so great that the capsule, stretched to its utmost, finally burst and the softened material almost filled the left side of the abdominal cavity.

CASE III.—Erichsen,⁹ 1861. A vigorous man, who had passed through typhoid fever and was almost ready to be discharged, suddenly collapsed and died "in a few minutes." The autopsy showed the abdomen to be filled with an enormous quantity of liquid and clotted blood. The pancreas was surrounded by a mass of clot as large as a child's head, which extended to the hilum of the spleen. The spleen formed a flaccid sac, seven inches in diameter, composed of grumous, confluent, livid-red parenchyma, in which no trace of normal splenic structure could be seen. In the region of the hilum were three or four tears about one inch in length. Liver was cirrhotic, enlarged, and anemic.

CASE IV.—Delafield,¹⁰ 1875. Boy aged eighteen years, two weeks before had caught cold; was seized with cough, fever, coffee-ground sputa; had a little pain in the right side of the chest. Was worse every afternoon. No diarrhea, headache, or epistaxis. October 27: Tongue clean; pulse, 100; temperature, $99\frac{3}{4}^{\circ}$; bowels regular; urine 1010, no albumin. Coarse rales over both lungs. October 29: Pulse, 100 to 112; temperature, $99\frac{3}{4}^{\circ}$ to $102\frac{1}{4}^{\circ}$. October 30: Pulse 114 to 122; temperature, 100° to $103\frac{1}{2}^{\circ}$. October 31:

⁷ Ruptur der vergrösserten und erweicherten Milz, Med. Zeit. des Vereins f. Heilkunde in Pr., 1839, No. 19; Ref. Schmidt's Jahrb., 1840, xxviii, 49.

⁸ Der Typhus in Mosjauer Militärspital während der Herbst und Wintermonate des Jahres, 1840-1841, Hufeland's Jour. der prakt. Heilkunde, 1843, xevi, 93.

⁹ Zwei Fälle von innerer Blutung, St. Petersburger med. Zeitsch., 1861, i, 71.

¹⁰ Through the courtesy of Dr. Delafield, these notes were copied from his case-book.

Pulse, 104; temperature, $100\frac{1}{4}^{\circ}$. November 1: Pulse, 96 to 120; temperature, 99° to $98\frac{1}{2}^{\circ}$. November 2: Pulse 98 to 120, temperature 99 to $98\frac{1}{2}^{\circ}$. November 3: Improving today, sat up. November 7: Complained of weakness; stayed in bed. November 10: Suddenly grew much worse. At 2 P.M., pulse, 145; temperature, $104\frac{1}{4}^{\circ}$. At 8 P.M., Pulse, 144; temperature, $105\frac{1}{2}^{\circ}$. November 11, at 2.30 A.M. patient was found in the hall dying. Died at 3 A.M. *Autopsy*: Brain had a slight increase of serum beneath; heart normal; lungs, moderate bronchitis; liver normal. Spleen weighed fourteen ounces with a large rupture extending all around it at about its middle. In the peritoneal cavity there was a large amount of blood. Large intestine normal. Along the entire length of the ileum solitary and agminated glands very much swollen and a few of them ulcerated. Small nodules in mucous membrane. Mesenteric glands very much swollen.

CASE V.—Wittmann,¹¹ 1876. Boy aged ten years. Admitted to the hospital on sixth day of illness. Persistent high fever, delirium, and bleeding from mouth and bowels. Tenderness over the cecum and spleen. Splenic dulness much increased. From the eighth day of illness on there was increasing tenderness of abdomen, especially in the region of the spleen. On the thirteenth day there was a rapid fall of the persistently high temperature to subnormal, symptoms of acute collapse, and death. *Autopsy*: The abdominal cavity contained one and one-half pounds of liquid and clotted blood. Spleen enlarged fourfold, soft and pale. On the outer border there was a tear one inch deep and two and one-half inches long, beginning near the hilum, running to the outer border, and ending on the upper surface. A second shallower and shorter tear began at the hilum, where it was joined with the first tear and extended down toward the tip of the spleen. Peyer's patches were swollen and in part ulcerated. The mesenteric glands much enlarged.

CASE VI.—Chrostowski,¹² 1885. Blacksmith, aged twenty-seven years. Had been ill several days when first seen. Temperature, 40.3° C.; pulse, 100; respirations, 24. Two days later became delirious; desperately attempting to get out of bed. Great tenderness in the region of the spleen. High temperature and rapid pulse and respirations. Abdomen enormously enlarged. Became unconscious during the night and died the next morning. *Autopsy*: The spleen was six times its usual size; the outside was covered with thick, dark blood. The vertical rupture of the spleen was 8 to 10 cm. long.

CASE VII.—Chrostowski,¹³ 1885. Male, aged eighteen years. Ill in bed six days before admission to the hospital. On twenty-

¹¹ Abdominaltyphus mit Milzruptur, Jahrb. f. Kinderheilk., 1876, ix. 329.

¹² Ruptures of the Spleen in General, and Two such Cases Occurring in Typhoid Fever, Hoyer-sche Denkschrift, Warschau, 1885 (Polish); Ref. Virchow-Hirsch, 1885, ii. 30.

¹³ Loc. cit.

second day the temperature still was high; patient was delirious. The next day the temperature fell to normal and the patient seemed better, but on the following day he died. *Autopsy* showed the spleen considerably enlarged and surrounded by thick, coagulated blood. The spleen showed a rupture of the capsule 3 cm. long, which extended into the splenic pulp.

CASE VIII.—Aaser,¹⁴ 1898. Man, aged twenty years. Patient had typhoid fever of fourteen days' duration, and died a half-hour after admission to the hospital. *Autopsy* showed a rupture of the spleen so extensive that a portion of the organ was almost completely severed from the rest.

CASE IX.—Kammerer,¹⁵ 1902. The patient was in the third week of typhoid fever. No trauma. Sudden restlessness and signs of internal hemorrhage. Diagnosis of intestinal perforation. *Operation*: Large amount of blood in belly. Intestine intact. Greatly enlarged spleen surrounded by clot. Capsule showed a tear four inches long, through which the splenic tissue protruded. Extirpation of spleen. Death after twelve hours. The rupture involved the capsule only.

CASE X.—Craig,¹⁶ 1904. Soldier, aged twenty-three years. Illness of eight days before admission to the hospital on September 12. Temperature reached normal before October 3. On that day the patient felt cold and sleepy. Temperature subnormal. Slight delirium. Next day had severe pain which was referred to the left hypochondrium. This pain increased on the following day. Gradual collapse and death on October 7. *Autopsy*: Typhoid ulcers in the ileum. Coils of small intestine were adherent and covered with purulent exudate. Appendix was inflamed. Spleen was greatly enlarged (20 by 11 cm.), and surrounded by a great mass of blood. Tear in the spleen was 3 cm. long and 1 cm. deep, from which the splenic tissue protruded.

CASE XI.—West and Dudding,¹⁷ 1906. Soldier, aged twenty-five years. Was admitted to the hospital on the third day of his illness. Fever ran a mild course, with few symptoms, until the ninth day (March 3), when at 8.45 A.M. he complained of severe pain in the middle of the abdomen. When seen fifteen minutes later he was in a collapsed condition, somewhat restless, with a rapid, weak pulse, and with the abdomen tender, distended, and tympanitic. Perforation was suspected. *Operation*: Abdomen was filled with blood. No perforation discovered. Spleen suspected as being the source of the bleeding, but because of the bad condition of the patient the abdomen was closed. Death occurred ten

¹⁴ Milzruptur ved tyfoidfeber, Tidskr. f. d. norske Laegefor, Christiania, 1898, xviii, 565.

¹⁵ Hemorrhage from the Spleen in Typhoid Fever, Ann. Surg., 1903, i, 288.

¹⁶ Rupture of the Spleen: Report of Two Cases, Med. News, 1904, lxxxiv, 780.

¹⁷ A Case of Enteric Fever with Spontaneous Rupture of the Spleen. Jour. Royal Army Med. Corps, London, 1906, vii, 183; Ref. Lancet, 1906, ii, 1230.

minutes later. *Autopsy:* Spleen was greatly enlarged, weighing two pounds two and one-half ounces. Capsule showed a tear three inches long on the diaphragmatic surface, and was extensively separated by a clot. Typhoid ulcers in the ileum and colon.

CASE XII.—Bryan,¹⁸ 1909. Man, aged thirty-one years. Was admitted to the hospital November 2 having been ill for one week with fever and headache. Complained of some pain on the left side under the ribs. Ran a persistently high fever for the next twelve days. No trauma. On the evening of November 14 the temperature became higher than usual (106°), and the pulse rapid and weak. The face was pinched; nose and extremities were cold, there was moderate dyspnea. The belly was hard, resistant, and tympanitic, but not distended. *Diagnosis:* Perforation and hemorrhage. *Operation:* The abdomen was opened along the outer border of the right rectus muscle. No perforation was found, although thickened Peyer's patches were evident. Blood in large quantities was found in the pelvis and in the region of the spleen. Spleen was removed. In spite of saline infusion and other measures to combat the shock and loss of blood, death followed one hour later. The spleen measured 18 by 9 cm., and weighed fourteen and two-third ounces. The rupture, situated at the lower pole, was stellate, everted, and crater-like. It covered an area 2.2 by 3.8 cm., and extended into the tissue of the organ.

A STUDY OF THE PATHOLOGY OF THE THYROIDS FROM CASES OF TOXIC NON-EXOPHTHALMIC GOITER.

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INTRODUCTION. That a secretion from the thyroid gland is the cause of the toxic symptoms in goiter has not yet been positively proved. Indeed, the proof is still somewhat incomplete that any secretion from the thyroid may be found in the circulating blood. However, evidence is slowly accumulating which it seems likely will ultimately prove both these propositions beyond peradventure.

Five years ago¹ I gave a detailed analysis of the pathology of 259 thyroids removed from patients listed clinically as "exophthalmic goiter" from January 1, 1905, to May 10, 1908, and,

¹⁸ Loc. cit.

¹ AMER. JOUR. MED. SCI., December, 1908, pp. 851-61.

in addition, a review of the pathologic reports of 35 cases similarly listed in the Mayo Clinic prior to January 1, 1908. I pointed out that above 76 per cent. of these glands showed primary parenchymatous hypertrophy and hyperplasia, and that in general, the length and severity of the case history could be predicated from a knowledge of the pathologic findings. The margin of above 20 per cent. of the cases on the "exophthalmic goiter" list whose thyroids did not show primary hypertrophy and hyperplasia of the parenchyma were explained at the time by the supposition that they were either "patients who have recovered from their toxic symptoms and are now suffering principally from long, previously acquired heart or nerve lesions," or that they were "recently developed, very mild, or moderately mild cases of long standing." The fairly accurate estimates of the clinical condition from the pathologic data were made on the hypothesis "that the symptoms of Graves' disease are associated with increased absorption of an increased secretion of the thyroid."

Since this report, it has become possible more intelligently to interpret the pathologic pictures because of the increasing clearness of our conception of the various clinical types of goiter. From an extensive and detailed study of all types of goiter, Plummer² has recently called attention to the fact that clinically there are two distinct groups of toxic goiters: (1) exophthalmic and the other (2) toxic non-exophthalmic. The former, I have demonstrated pathologically, all show primary hypertrophy and hyperplasia of the parenchyma as the dominant pathologic change in the thyroid. Allowing for a small margin of error on both the part of the pathologist and of the clinician, all cases of clinically exophthalmic goiter coming to operation in the Mayo Clinic during the years 1911 and 1912 showed primary hypertrophy and hyperplasia of the parenchyma of the thyroid and practically no cases of toxic non-exophthalmic or of non-toxic (*i. e.*, simple) goiter showed any such pathologic change.

Thus the evidence of the constant association of primary hypertrophy and hyperplasia of the thyroid with the symptoms of true exophthalmic goiter would seem to be fairly conclusive. Our previous communications have, however, touched but lightly on the pathology of the thyroid in cases of toxic non-exophthalmic goiter, and it is this phase of the subject to which I wish herein to call attention.

Plummer² has shown that about 23 per cent. of all goiters reported as non-hyperplastic are of the toxic non-exophthalmic type, while the remainder are atoxic (simple) goiters. He notes, further, that "Patients coming under observation with non-hyperplastic toxic goiter give a history of having first noticed the goiter at the average

² Jour. Am. Med. Assoc., August 30, 1913, pp. 650-51.

age of twenty-two years and the evidence of intoxication at the average age of 36.5 years. The corresponding ages for hyperplastic goiter are respectively 32 and 32.9 years. That non-hyperplastic goiter is noted ten years earlier in life than hyperplastic goiter, and that 14.5 years elapse between the appearance of non-hyperplastic goiter and the development of notably toxic symptoms, while the constitutional symptoms are noted but a few months later than the goiter in patients affected with hyperplastic goiter, is alone sufficient to show that we are dealing with at least two distinct pathologic and clinical groups. That one is not the sequence of the other is self-evident."

Plummer further divides the intoxications from non-hyperplastic goiter into two merging groups: "(1) A group in which the cardiac toxin predominates and in which the clinical picture closely resembles, and, in many instances, cannot be differentiated from, the cardiovascular complex resulting from alcoholic,luetie, septic, and other well-known toxins; (2) A group more closely presenting the picture of Graves' disease and including the cases that have been erroneously so diagnosed by the mass of the profession."

I wish to present in this paper the results of a somewhat intensive study of the thyroids from approximately equal numbers of cases taken consecutively in our series, the only selection being made consisting in the exclusion of cases of which full data were not at hand. This includes:

1. 431 thyroids removed from cases of true exophthalmic goiter during the years 1911 and 1912.

2. 373 thyroids removed from as many cases of non-toxic (*i. e.*, simple) goiter during the year 1912.

3. (a) 129 thyroids removed from toxic non-exophthalmic cases during the years 1910, 1911, and 1912, and clinically in Plummer's sub-group 2, *i. e.*, "cases with symptoms closely approaching the picture of Grave's disease," (b) 155 thyroids removed from toxic non-exophthalmic cases during 1911 and 1912, and clinically in Plummer's sub-group 1, *i. e.*, "cases in which the clinical picture closely resembles and, in many instances, cannot be differentiated from the cardiovascular complex resulting from alcoholic,luetie, septic and other well-known toxins", and (c) thyroids from 90 cases similar to the last but of more mild or doubtful toxicity. The non-exophthalmic cases of clinical group 2 were included on the "exophthalmic goiter" list for 1910, 1911, and 1912 because of their resemblance to true exophthalmic goiter, while the cases in clinical group 1 were included on the "simple goiter" list because, though toxic, they did not resemble symptomatically the cases of true exophthalmic goiter. The thyroids from these cases have all been carefully analyzed as to their gross and microscopic pathology. A summary of the more important analytic data is presented in the following table:

COMPARISON OF PATHOLOGIC GROUPING OF THYROIDS FROM CASES OF EXOPHTHALMIC, TOXIC NON-EXOPHTHALMIC, AND ATOXIC (SIMPLE) GOITER.

	Percentage distribution.					Average age at operation.					Average duration of goiter before operation.					Average weight of portion of gland removed.										
	Exoph. goiter.	Toxic goiter clinic, Group 2.	Toxic goiter clinic, Group 1.	Toxic goiter clinic, Group 1. + Group 2.	Atoxic (simple) goiters.	Exoph. goiter.	Toxic goiter clinic, Group 2.	Toxic goiter clinic, Group 1.	Toxic goiter clinic, Group 1. + Group 2.	Atoxic (simple) goiter.	Exoph. goiter.	Toxic goiter clinic, Group 2.	Toxic goiter clinic, Group 1.	Toxic goiter clinic, Group 1. + Group 2.	(Atoxic simple) goiters,	Exoph. goiter.	Toxic goiter clinic, Group 2.	Toxic goiter clinic, Group 1. + Group 2.	Toxic goiter clinic, Group 1.	Toxic goiter clinic, Group 1. + Group 2.	Grams.	Grams.	Grams.	Grams.	Atoxic (simple) goiter.	
A Early primary parenchymatous hypertrophy and hyperplasia	4.0	25.0	0.3
B Advanced primary parenchymatous hypertrophy and hyperplasia	43.0	31.7	0.9
C Regressing primary parenchymatous hypertrophy and hyperplasia	52.5	40.7	3.5
Average of total parenchymatous hypertrophy and hyperplasia	99.5	0.5	35.9	2.3
D Secondary regeneration of atrophic parenchyma of "colloid" goiter	50	17	9	9.0	..	34.0	32.0	38.0	31.0	..	6.9	15.3	8.0	9.6	..	67.0	100	153	143.0
E Fetal adenomas	12	7	10	5.0	..	39.0	47.0	39.0	38.0	..	4.4	5.8	13.6	12.5	..	68.0	97	139	122.0
F Decenerating fetal adenomas	33	14	18	18.0	..	43.0	50.0	48.0	40.0	..	12.6	22.7	24.2	13.1	..	91.0	186	190	129.0
Average of total fetal adenomas	45	21	28	23.0	..	41.0	48.9	44.7	39.7	..	8.8	18.0	20.5	13.0	..	83.7	162	172	127.5
G Adult "colloid" adenomas	3	21	19	23.0	..	45.0	44.0	43.0	39.0	..	17.7	15.2	14.5	14.3	..	139.0	184	206	147.0
H Atrophic parenchyma, "colloid" thyroids, "adenomatous," etc.	2	41	44	44.0	..	52.0	46.0	41.0	37.0	..	12.0	20.2	16.5	14.5	..	140.0	196	188	164.0
Average of total colloid goiters, adult parenchyma	5	62	63	67.0	..	47.5	45.0	41.6	37.5	..	14.0	18.7	16.0	14.4	..	139.0	192	193	159.0

DISCUSSION OF DATA. *Percentage Distribution.* The distribution of the thyroids from each of the four clinical groups into the eight pathologic groups shows the following interesting points:

1. Practically all of the 433 cases of true exophthalmic goiter show some stage of primary hypertrophy and hyperplasia; of the thyroids; 4 per cent. are in an early stage, 43 per cent. in an advanced stage, and 52 per cent. in a regressing stage. As I have previously pointed out,³ this regression may be due to (a) the self-destruction of the parenchyma of the gland through the over-functioning of hyperplastic tissue, or (b) the destruction of the parenchyma through surgical interference (*e. g.*, ligation of the thyroid arteries which had been performed in a large percentage of the cases in this series).

2. Fifty per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 (*i. e.*, those which resemble more or less the true exophthalmic goiter cases) showed marked evidences of regeneration of the parenchyma (group D). I have elsewhere noted that regeneration of previously atrophic parenchyma of the thyroid is often a marked process which can usually be differentiated from primary parenchymatous hypertrophy and hyperplasia by (a) the abundant presence of atrophic parenchyma within large acini, (b) the development of numerous new acini within one or more portions of the walls of the old large colloid-filled acini and which early fill with dense colloid, and (c) the development of multiple layers of relatively small parenchyma cells within the large colloid-filled acini, which are distinguished from primary parenchymatous hypertrophy and hyperplasia by the smaller size of the parenchyma cells and the absence of papillæ.

3. Seventeen per cent. of the thyroids from the positively toxic cases in clinical group 1 (*i. e.*, those in which the clinical picture appears to be the result of a cardiac toxin) are of the regenerative (D) type. Though this percentage is but one-third that of the preceding group, it is still nearly twice that shown by the thyroids of doubtful toxicity and by the atoxic (simple) goiters, both of which gave the same (9 per cent.) in the regenerating (D) class.

4. Twelve per cent. of the thyroids from the toxic non-exophthalmic cases of clinical group 2 are early fetal adenomas and 33 per cent. degenerating fetal adenomas, making 45 per cent. in all in which the pathology is that of encapsulated adenomas made up of acini of largely lumenless type. This leaves but 5 per cent. of the cases in clinical group 2 in which the pathology of the thyroid is that of colloid goiters, with adult parenchyma. This is in strong contrast to the distribution of the thyroids in the toxic cases from clinical group 1, in the positive ones of which only 7 per cent. of the thyroids are early fetal adenomas, 14 per cent.

³ AMER. JOUR. MED. SCI., December, 1913, 781-90.

degenerating fetal adenomas (21 per cent. in all), while 62 per cent. of the thyroids in this clinical group 1 are colloid goiters with adult parenchyma. This distribution is closely followed by the thyroids in the questionable toxic group—E, 10 per cent.; F, 18 per cent.; G, 19 per cent.; H, 44 per cent. respectively—which also is almost parallel with the distribution of the thyroids from the non-toxic (simple) goiters—E, 5 per cent.; F, 18 per cent.; G, 23 per cent.; H, 44 per cent. This may all be summarized by saying that one-half of the thyroids from the toxic non-exophthalmic cases which more closely resemble true exophthalmic goiter (clinical group 2) are of the regenerative type, and nearly all the remainder are fetal adenomas, while, in contrast to this, only one-eighth of the thyroids from the toxic non-exophthalmic cases which do not resemble true exophthalmics (clinical group 1) are of the regenerative type, less than one-fourth are fetal adenomas and more than three-fifths of them are adenomas or colloid adenomatosis, with adult and atrophying parenchyma.

Average Age Distribution. Plummer has shown that patients with true exophthalmic goiter first notice the excessive development of the thyroid at an average age of 32 years, with evidence of intoxication developing 0.9 of a year later. The average age of these patients at the time of the removal of the thyroid was 25 years, in those cases in which the parenchyma of the thyroid was found to be in an early stage of primary hypertrophy and hyperplasia (pathologic group A), 31.7 years in those cases in which it was in an advanced stage of primary parenchymatous hypertrophy and hyperplasia (pathologic group B), 40.7 years in those cases in which it showed regressive changes secondary to primary hypertrophy and hyperplasia of the parenchyma (pathologic group C), or an average of 35.8 years for all cases in the group. The average age of the patients in clinical group 2 of the toxic goiter cases is lowest in those whose thyroids were of the regenerative type and highest in those whose thyroids were colloid goiters with adenomas or adenomatosis. This same is true throughout the other two groups of toxic goiters. It is worthy of note that the average age of the patients with toxic symptoms in both clinical groups is considerably higher than the average age of the patients with non-toxic symptoms in each of the pathologic groups. This is capable of several interpretations, the more obvious of which are (a) regenerations of atrophic epithelium (group D) require considerable time for the development of symptoms; (b) fetal adenomas on the average require more time for the development, if ever, of toxic symptoms than do regenerations; (c) adult adenomas and diffuse adenomatosis are slowest of all types to develop, if ever, toxic symptoms. In general, it may be said that patients with non-exophthalmic goiters either come to operation before they have

developed their toxic symptoms at an average age of from thirty-one to forty years according to their pathologic classification, while patients with toxic non-exophthalmic goiters come to operation at an average age of from thirty-two to fifty-two years, according to their pathologic grouping. It is important, however, to control our deductions from a study of the average ages at operation by a consideration of the date of the next classification.

Average Duration of Goiter before Operation. The average duration of goiter before operation in the cases of true exophthalmic goiter is 0.3 year for those in which the thyroid was of pathologic group A (early primary parenchymatous hypertrophy and hyperplasia), 0.9 of a year in those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia) and 3.5 years in those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia). In the toxic cases of clinical group 2 the goiter had existed 6.9 years in those of pathologic group D (regenerations), 4.4 years in those of pathologic group E (early fetal adenomas) 12.6 years in those of pathologic group F (degenerating fetal adenomas), or an average of 8.8 years of the total fetal adenomas—and 14 years in those in which the thyroids were of pathologic groups G and H (colloid goiters with adult parenchyma). When the first of these figures are compared with the average duration of the goiters in the other groups, it would appear that those cases in clinical group 2 (*i. e.*, toxic goiters resembling exophthalmics) though they develop later in life, as shown by the average ages at operation, yet are of sufficient intensity to bring the patients to operation considerably earlier than patients of clinical group 1 or those of the atoxic group.

Average Weight of Portion of Gland Removed. The average weight of the portion of gland removed is in general a fair relative index of the total size of the thyroid. The examination of the average of these weights for thyroids in the different groups shows that of those from cases of exophthalmic goiter, those in pathologic group A (early primary parenchymatous hypertrophy and hyperplasia) are the smallest, 38 grams, those of pathologic group B (advanced primary parenchymatous hypertrophy and hyperplasia) are considerably larger, 61 grams, and that those of pathologic group C (regressing primary parenchymatous hypertrophy and hyperplasia) are smaller than the preceding, 51 grams. In those from clinical group 2 (toxic non-exophthalmics), those of groups D and E are much smaller than those of any of the other groups, 67 and 68 grams respectively. This observation is in harmony with the conclusions to be drawn from the average durations of goiter since these relatively smaller glands are those not so much blocked with retained colloid as are the thyroids of the simple goiter type. Indeed, throughout this clinical group 2, the average weight of

the glands of each of the pathologic groups is very much smaller than the average weight of the glands in parallel pathologic groups of either clinical group 1 or of those of the simple goiters.

General Summary. 1. The pathology of the thyroid in true exophthalmic goiter is essentially a primary parenchymatous hypertrophy and hyperplasia, *i. e.*, an increased amount of functioning parenchyma associated with an increased absorption. The process is an acute one.

2. The pathology of atoxic simple goiter is marked essentially by atrophic parenchyma, decreased function and decreased absorption. The process is a chronic one.

3. The pathology of toxic non-exophthalmic goiter of clinical group 2 (*i. e.*, those resembling exophthalmic goiter) is one of increased parenchyma through regenerative processes in atrophic parenchyma or the formation of new parenchyma of the fetal type, with an increase in each instance of secretory activity and of absorption. The process is a chronic one, but sufficiently active to cause the patient to consult a surgeon earlier than do those patients in clinical group 1.

4. The nearer the cases of clinical group 2 (toxic non-exophthalmics) approach, in age and symptoms, true exophthalmic goiter, the shorter the duration of the period of goiter before operation and the smaller the average weight of the gland at the time of its removal.

5. The cases of toxic goiter of clinical group 1 (*i. e.*, those in which the symptoms are of the cardiovascular variety) much more closely resemble cases of simple goiter in their pathology in all respects than do the cases of clinical group 2. A larger number of them are of the colloid goiter type, the enlargement of the thyroid has existed for a longer period before operation, and the portion of the gland removed is materially larger than in those cases of clinical group 2.

6. Finally, it may be stated that all the above pathologic evidence points to a constant relative association of increased secretion and increased absorption from the thyroid proportional to the degree of toxicity on the part of the patient. We have as yet no absolute proof that such secretion and absorption is the cause of, rather than coördinate with, the symptoms, but the presented evidence strongly points to that conclusion.

THE STUDY OF RENAL FUNCTION: THE PROGNOSTIC VALUE OF STUDIES OF RENAL FUNCTION.¹

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DESPITE the increased light shed upon medicine generally by science, the aphorism of Hippocrates holds true today, "experience is fallacious and judgment difficult." Constant daily contact with nephritis in ward rounds, interspersed with occasional visits to the pathologist, serves to convert such an opinion into a conviction. Even the best clinical training and experience do not fully equip the physician to cope successfully and authoritatively with the problem of prognosis in certain cases of nephritis, nor do they reveal the exact status of his patient in many other pathological conditions of the kidney. To his assistance then are lately brought renal functional tests.

The ultimate object of any line of work is often furthered by a temporary abandonment of the consideration of details concerned in its various phases, and the replacement of this by reflection upon it in its entirety and in its relationship to its environment. A comprehensive review of any field of research, particularly in regard to its relationship to the fundamental sciences involved, and in regard to the absolute advancement resulting from it, is seldom amiss, since it often results in the disclosure of the uselessness and limitation of certain procedures, suggests new and better methods of attack, and establishes a truer conception of the purport and importance of the work.

The development and introduction of numerous renal functional tests are in accord with the general trend of medicine of today, the importance of knowing the ability of any organ to carry on its work, rather than the appearance of the cells engaged in the work, being even more emphasized.

Determination of renal function is of vital interest alike to the internist and surgeon from the standpoints of diagnosis, prognosis, and treatment. The widespread nature of the importance of such determinations is probably not so apparent to those confining their attention purely to its medical or surgical aspect, but to those interested in methods of determining renal functional capacity as such it becomes firmly impressed as investigations are made in relation to acute and chronic nephritis, orthostatic or other albuminurias, arteriosclerosis, uremia, myocardial insufficiency, polycystic kidneys, obstruction in the lower urinary tract, cystitis,

¹ Part of a symposium on Renal Function at a meeting of the Congress of American Physicians and Surgeons held in Washington, D. C., May 6, 1913.

pyelitis, unilateral and bilateral hydronephrosis, pyonephrosis, pyelonephritis and ureteral renal calculi, hypernephromas, renal tuberculosis, and the numerous allied conditions calling for differential diagnoses.

The clinical diagnosis made in any individual case, before offering a prognosis certain problems must be investigated: (1) What pathological condition underlies the clinical picture? (2) Is the condition localized to the kidney or is any other system (cardio-vascular) involved or likely to be involved? (3) What is the functional capacity of the kidney? Is this permanent or temporary, and subject to change? (4) Is or is not the condition amenable to treatment? Only by attention to all these factors can anything approaching correct prognoses be attained.

Renal functional capacity is usually ascertained in one of two ways: (1) Tests of excretory capacity through the quantitative determinations of the excretion of various substances in the urine, dyes—methylene blue, indigo carmine, rosaniline, sulphonaphthalein, other chemicals—potassium iodide, lactose, salicylates, sodium chloride, urea, sugar following phloridzin, and the enzyme diastase. (2) Tests of retention through quantitative determination of the concentration of certain substances in the blood, ions through electrical conductivity, molecules through cryoscopy, urea, incoagulable nitrogen, and cholesterin.

The recent work of Folin and Denis indicates that the concentration of urea, 0.5 gm., and of total incoagulable nitrogen, 0.6 gm. per liter, heretofore considered normal, must no longer be so considered, since in sixteen strictly normal individuals the highest non-proteid nitrogen which they found was 26 mg. and urea nitrogen 13 mg. per 100 gm. blood. Slight nitrogen retention may apparently occur in many diseases, but in our experience, with a large number of cases, using the older methods and also Marshall's new urea method, we feel that no great prognostic significance is to be attached to urea concentrations less than 0.55 and total incoagulable nitrogen 0.5 gm. per liter. Greater concentrations than this, together with a serum freezing-point lower than -60° , are of the greatest prognostic importance. Evidences of retention reaching this degree we refer to as cumulative phenomena.²

These test all prove of value prognostically, but some much more so than others. Those of most importance in Group I are the dye substances, especially the phthalein, and of Group II, cryoscopy, total incoagulable nitrogen, and urea. The phthalein test is of prognostic value in all pathological conditions, whereas

² One would expect the urea and total incoagulable nitrogen in the blood to be approximately inversely proportional to the excretory efficiency of the kidney since this is the only channel of elimination (practically speaking) for the nitrogenous waste products.

certain cases of severe nephritis even in uremia show no marked increase in incoagulable nitrogen or urea. So the presence of cumulative phenomena is of the greatest prognostic significance, while their absence is not.

Functional studies reveal only the excretory capacity of the kidney. By themselves they do not make the diagnosis or settle the prognosis. Just as routine blood examinations occasionally reveal an unsuspected leukemia, the routine use of functional tests brings latent kidney involvement to light. These tests should be used routinely in conjunction with other procedures to aid in diagnosis, prognosis, and selection of lines of treatment. Their importance in different cases varies. It is possible that a series of ten or twelve different tests may add little or nothing to our knowledge of the condition after a careful clinical study, whereas after equally as careful a clinical study one test, verified, may change all of our ideas concerning the diagnosis, prognosis, and treatment; as for instance in one of our cases where a boy, prior to functional studies, was considered the subject of a diabetes insipidus, with an excellent immediate prognosis, and after one phthalein test was recognized as a case of advanced chronic interstitial nephritis verging on uremia, which was substantiated at autopsy within two weeks. Because of our inability to determine in advance in what cases the functional studies will be of value, their routine employment becomes of paramount importance.

Clinical or functional studies alone are inadequate from the standpoint of prognosis. The application at any one time of one or a series of functional tests reveals only a limited amount of information, *e. g.*, the excretory power of the kidney at that particular time. This, apart from other considerations, may be of no great prognostic significance. In order to become so the data from such studies must be considered in conjunction with a careful clinical study, and the underlying pathological processes responsible for the clinical and functional pictures must be recognized, identified, and understood.

Aside from or in the absence of clinical studies, repeated functional estimations, with the employment of the appropriate test over a varying period of time, will reveal the nature (stationary, progressive, retrogressive) and degree of renal involvement, and so prove of prognostic value. But even repeated functional studies prove of greatest value when associated with careful clinical studies, for it has been definitely established that functional pictures carry different significance in various pathological (clinical and experimental) associations. Diseases may be functionally identical, clinically and prognostically different, and *vice versa*. To illustrate, a low condition of function, as indicated by a low phthalein output, together with marked delay in the excretion of chlorides, iodide, and lactose, may be encountered in experimental

chromium nephroses or in marked passive congestion (experimental or clinical). This may be followed within a week by a practically normal renal function owing to regenerative processes in the first instance and to the reëstablishing of cardiac compensation and better circulation in the second, whereas findings identical with those originally encountered, occurring in a case of chronic interstitial nephritis, indicate impending uremia and a grave prognosis. Again, identically low functional capacity in cases of urinary retention associated with pyelonephritis and hydro-nephrosis on the one hand, and in chronic nephritis on the other, do not have the same prognostic significance, since the surgical condition is amenable to treatment, whereas no efficient therapy is at hand in chronic nephritis. From this the necessity of understanding the absolute significance to be attached to the findings of any functional test becomes apparent. Lepine has objected to the employment of any one substance for the purpose of estimating functional capacity of the kidney, on the ground that the kidney does not excrete all substances with the same facility, and that data obtained from a study of the excretion of one substance, therefore, cannot be applied to others. He believes that each substance has its own coefficient of excretion. That there is not accurate and exact parallelism of excretion of all substances by the kidney, one is forced to admit, but that there does exist a certain degree of parallelism, the same general tendency of excretion for all of the substances so far used, is unquestionably true. The difference is one of degree. *Familiarity with the meaning of these variations in degree, to which peculiar prognostic significance attaches, is most desirable therefore.*

The value of any of these excretory tests is purely empiric, because of lack of sound physiological information dealing with the ultimate physics and chemistry of the excretion of any substance by any part of the kidney tubules or glomeruli. Experience has taught us that the failure of phthalein to appear in the urine or its excretion in mere traces in the course of chronic nephritis indicates impending uremia and grave prognosis, even in the absence of any definite knowledge concerning the excretion of any other substance. In other words, failure to excrete phthalein empirically signifies incapacity on the part of the kidney to carry on its work, hence a bad prognosis. But this does not hold for all substances. Failure to detect diastase in urine by the customary technique employed means renal injury, possibly severe renal injury, but not necessarily so.

How can we utilize functional tests to the greatest advantage prognostically?

1. The prognostic value of functional studies must be considered from two points of view: (a) As to the immediate outcome (days, weeks, or months are here concerned); (b) as to the ultimate fate

of the patient and the future course of the pathological processes. At present their value from the first point of view is definitely established, and is here discussed in its various phases. Prognostic significance other than immediate will be revealed only in the course of years. In association with Dr. Thayer and Dr. Baetjer an attempt is being made to learn of the condition through correspondence and reëxamination where possible of all of our patients previously studied. Data sufficient for conclusions are not yet at hand. Surgically, little prognostic value other than immediate, can be considered, since surgical interference so radically changes the condition.

2. We need a much greater familiarity with the significance and reliability of the findings of all these tests in all renal lesions, experimental and clinical, medical and surgical.

3. We must learn the relative ease with which each and every approved test responds to increasing degrees of injury of any type, such information as has been presented in experimental nephroses by Schlager and his co-workers, by Pearee, Austin, and Eisenbrey, or in chronic passive congestion in more recent studies.

4. Experimentation and clinical experience must teach us upon which tests reliance as to prognosis can be placed in each and every type of renal disease.

5. We need a much deeper insight into the nature of the processes at work in certain diseases, *e. g.*, eclampsia, kidney of pregnancy, certain types of nephritis, etc. We must learn whether certain symptoms, conditions, and phenomena are actually due to the accumulation of toxins, ferments, etc., whether this accumulation does result from the failure on the part of the kidney to excrete them, or whether the kidney is the usual channel of their excretion. May not, for instance, certain of these phenomena be the expression of deprivation of the body of certain substances through excessive excretion through hyperpermeability? More light is needed on the factors responsible for hypertension, edema, uremia, etc. *We must learn to recognize in what conditions the excretory power of the kidney is a real criterion to the patient's actual condition.* Prognostically their value will thus be enhanced through a knowledge of the limitations of these tests.

6. Functional tests will become more generally used, and hence of more value when we know which ones can be discarded without loss and which combination of tests (the smaller, the better) will yield all the information necessary in any given type of disease.

VALUE IN MEDICAL CASES. Until recently little or no prognostic value has been attached to functional studies in medical cases, although their worth in this connection is fully as great as in the surgical. The introduction of new tests, notably the phthalein, and improvements in the technique relating to the old ones are largely responsible for the change in the attitude of the

profession. The limitations of the value of such tests must be clearly recognized. In all forms of renal disease a prognosis only so far as renal efficiency or inefficiency can be made through their use. Death may occur from innumerable other factors, concerning which they give no information.

In *acute nephritis* the prognosis is largely dependent upon the etiology. When associated with specific fevers it becomes impossible to ascertain whether the patient is suffering from a toxemia due to non-excretion or one due to a specific toxin of the fever. The capacity of the kidney to excrete can be readily determined, but this means but little prognostically on account of the rapidity with which marked changes in this respect occur. Clinically we have seen cases without 10 per cent. phthalein output for two hours excrete 28 per cent. four days later and the normal amount within two weeks. Experimentally, chromium animals with a zero output for two hours have returned to a normal excretion within ten days, while twenty-four hours later, more chromium having been given, the phthalein was again not excreted. It is evident, therefore, that frequent repetitions of tests are essential to prognosis in acute nephritis. But when a patient exhibits, as one of ours did, no phthalein, no lactose, together with a high blood urea concentration, the case must be considered a grave one, though not hopeless. The immediate danger from the renal inadequacy factor is at least determined.

The functionally mild nature of a *chronic nephritis* is readily recognized. Associated with the albumin and casts, a slight increase in blood pressure, palpable vessels (arteriosclerosis?) and slight cardiac hypertrophy, there may be encountered a somewhat delayed lactose and phthalein excretion, a normal total salt output, with a vascular hyposthenuria, but no evidence of cumulative phenomena. In such a condition the immediate outlook is favorable, but tests should be applied intermittently to determine whether the condition is stationary or progressive and the rate of progression. In prognoses caution should be observed on account of the possibility of acute exacerbations becoming superimposed on the chronic process. Aside from this the case may develop gradually into an advanced nephritis, with marked renal insufficiency exhibiting uremia, into a nephritis with a cardiac insufficiency or with a vascular accident (apoplexy).

Advanced nephritis is indicated always by decreased excretory capacity and usually by cumulative phenomena. Although clinically it is difficult often to determine the severity of the condition, this is readily obtained through functional studies. Perhaps the majority of cases of chronic interstitial nephritis are clinically latent, unrecognized until the occurrence of serious or even fatal complications. Uremia clinically may appear to come out of a clear sky, whereas its unsuspected proximity can be readily recog-

nized and its occurrence can be easily predicted through functional studies. In chronic nephritis, failure on the part of the kidney to excrete phthalein or lactose, together with marked cumulative phenomena, indicates renal insufficiency, impending uremia, and calls for a grave prognosis.

Other cases with marked clinical nephritis, even with mild uremia, but with less marked functional involvement, may be more difficult for prognosis. Many factors must be considered. Will the heart dilate? Will an apoplexy occur? Will an acute attack be superimposed? But so long as the renal function remains fair, say 30 per cent. phthalein for two hours, with cumulative phenomena absent, and none of the above complications arise, death from renal insufficiency, uremia, is not at all likely, and an immediate favorable prognosis can be given. Care must be used in predicting more than this. The tests should be repeated in order to follow the course of the disease.

That a good or normal phthalein output is occasionally encountered in the presence of definite nephritis has been pointed out in our earlier publications. At the same time the absence of hyperpermeability to phthalein in all our studies was commented upon. Pepper and Austin have lately called attention to a case of nephritis with marked albuminuria, cylindruria, and edema in which the phthalein and total incoagulable nitrogen were normal, while the chloride output after additional salt was somewhat delayed. The phthalein output in this case, 67 per cent. for one hour, strongly suggests hyperpermeability. Baetjer in our clinic has encountered four cases during the winter which clinically and functionally resemble Pepper and Austin's case, and in all of which hyperpermeability to phthalein and lactose was strongly suggested. This type of nephritis is not well understood. Since all of the patients studied are still living, the nature and extent of the anatomical lesions are as yet undetermined, and the value or significance of functional studies in relation to them is not clear. Since the patients have continued to live, the tests furnished correct information so far as immediate prognosis at least is concerned.³

CARDIORENAL CASES. All grades of nephritis and myocardial insufficiency may be associated, and only through the use of clinical and functional studies can the cases be properly interpreted. By the combined studies it is possible in any given case to determine the relative responsibility of the kidney and heart from the clinical picture presented, and thereby to arrive at a better prognosis.

Experimentally it has been shown that in moderate degrees

³ It is possible that this increased permeability is not a passive condition but an active functional response to some unknown renal stimulant, which differs essentially from an ordinary diuretic.

of passive congestion the excretion of lactose, iodide, and salt may be delayed, while the phthalein output remains normal. When the congestion is more severe the phthalein is decreased, but returns to normal with the earliest signs of improvement of circulation. Strauss and Hohlweg found that incoagulable nitrogen and urea of the blood are increased in chronic passive congestion, but not so strikingly as in nephritis, findings which we are able to corroborate. Low phthalein and the cumulative phenomena, therefore, bear great prognostic and diagnostic significance in this group of cases, since they are only encountered with rather advanced nephritis or with a severe passive congestion calling for a grave prognosis.⁴

Moderately advanced nephritis associated with a moderate myocardial insufficiency often exhibits a fair renal capacity, in which case the prognosis rests more on the response of the heart to treatment than on the nephritis. An increase in the phthalein output may be the first evidence of restoration of cardiac compensation, and hence it indicates a favorable immediate prognosis. The absence of cumulative phenomena, together with a fair phthalein output in any clinically severe cardiorenal disease, points to the heart as the responsible factor.

A low excretory capacity, with marked increase in blood urica or total incoagulable nitrogen or a low serum freezing-point, indicates either that the kidneys chiefly must be considered etiologically or that the heart is in an extremely precarious condition; in either case the prognosis is grave. With or without cumulative phenomena a low excretory capacity persisting after clinical evidence of cardiac improvement indicates severe nephritis and an unfavorable prognosis.

MYOCARDIAL INSUFFICIENCY. Marked renal insufficiency may result from pure chronic passive congestion. Exceptionally, clinically and experimentally, the functional studies reveal a decrease in function equaling that seen in the severe grades of nephritis. Since the congestion for this must be of a most extreme grade, death is imminent on account of the heart. As a rule in myocardial insufficiency, with a symptomatic and urinary picture identical with that seen in a moderately advanced nephritis alone or in nephritis associated with a cardiac break, renal function as indicated by both excretory and retention tests is surprisingly good. When low renal function is followed by an increased phthalein output the amount of increase gives a fair approximation of the extent of cardiac improvement.

POLYCYSTIC KIDNEYS. All conditions of renal function may be here encountered and a prognosis can be based upon functional

⁴ In pure chronic passive congestion we have never seen the rest nitrogen higher than 0.63 gm. per liter.

findings in this condition just as in chronic interstitial nephritis. A case has been reported exhibiting a normal function, death resulting from an intercurrent disease, while a zero phthalein was found by Pepper and Austin in a case dying in uremia. A case now under observation, the diagnosis being confirmed by collargol skiagram, has a fair function only, 20 per cent. phthalein for two hours.

SURGICAL CASES. Uremia after operation has been responsible for a large proportion of the mortality in renal surgical cases, so that any method capable of furnishing information as to the probability of the occurrence of such a condition is of great importance to the surgeon.

Emphasis upon one point is needed, viz., a fair or a normal renal function must not be interpreted as meaning that uremia or anuria will absolutely not develop after operation, or as meaning that the postoperative function will be the same as that before surgical interference. Many accidents may occur. The subject of a perfectly normal function may, after operation, develop anuria and die, although other things being equal he is much less apt to do so than a patient who prior to operation has a low renal capacity. The great value of these studies surgically lies in their ability to reveal those cases which are suitable and those which are unsuitable for operation so far as the kidneys are concerned. They indicate that uremia is certain to occur following operation in a given case, that certain cases are hopeless, others poor, good, or excellent surgical risks, but they offer no absolute security that the subject of a good surgical risk will not develop renal insufficiency.

The previous knowledge of the renal function is also of prognostic importance in the event of development of postoperative uremia, for the occurrence of this condition in one who has been previously shown to have a continuously low function means a grave prognosis, whereas in one who has had a good renal function recovery is more probable.

The tests are of value in two classes of cases: (1) Those with retention of urine, renal injury following, due to obstruction in lower urinary tract, with back pressure upon the kidney resulting in functional changes, in hydronephrosis, or in pyelonephritis, etc., and (2) those with unilateral or bilateral renal disease.

OBSTRUCTION IN LOWER URINARY TRACT. As a result of obstruction in the lower urinary tract, pathological changes may occur in the ureter and kidneys, dilatation of the ureters, varying grades of hydronephrosis, and, as a result of the long-continued high pressure, atrophy of the parenchyma of the kidney. Not infrequently infection occurs with the development of a pyelitis, a diffuse or localized pyelonephritis, or pyonephrosis. The occurrence of these complications is often difficult of recognition, and is often overlooked, especially in the absence of symptoms of

renal inadequacy. Cystitis and associated albuminuria and cylindruria are usually present, albumin and casts not contra-indicating operation. The urinary output may be normal in many instances, also the urea output and total solids, and yet the patient be on the verge of renal failure. Diastrous results may be certain to follow any radical surgical intervention at this time, yet often nothing outside of functional studies can furnish this information.

A marked decrease in the excretory phenomena alone or associated with cumulative phenomena means severe derangement of renal function which may be of either a temporary or permanent character. No prognosis should be given, and, except in emergency or where the surgical procedure employed is the only method of improving or relieving the renal disturbance present, no surgical interference attempted without further study in conjunction with suitable preliminary treatment (Young's treatment, catheter drainage, and abundance of water). Under this regimen repeated tests will quickly demonstrate the nature of the derangement, cases of nephritis and of true interstitial destruction showing no improvement, whereas purely functional changes or those secondary to pyelonephritis show markedly increased function.

This constitutes a striking group of cases. A patient in uremia, with low excretory functional findings and with cumulative phenomena, may in the course of a few weeks return to an excellent clinical condition, with a renal functional capacity approaching normal. Only one such experience is necessary in order to impress upon physician and surgeon the importance of determining (through time, preliminary treatment, and repetition of tests) the nature of the depressed function, temporary or permanent. The prognosis of the operation, so far as uremia and anuria are concerned, is infinitely better in those cases showing marked improvement in renal function following the adoption of the preliminary treatment above mentioned.

All tests are not of equal prognostic value in this group of cases. The phthalein had already established its place. Lactose is of no significance, since its total suppression is frequently encountered when the phthalein, diastase, cryoscopy, blood nitrogen, and urea all show a fair or moderately good renal function, the truth of which is demonstrated in the subsequent history. In a series of twenty such cases, lactose was recovered in the urine in only six instances. Glycosuria following phloridzin is also slow in appearance or fails to appear at all. These two tests, therefore, exaggerate the degree of functional changes and bear no prognostic significance.

The phthalein test along with cryoscopy, urea, and non-proteid nitrogen determinations of the blood, gives a sharp index of the functional capacity.

UNILATERAL AND BILATERAL SURGICAL DISEASES. The prognosis in unilateral and bilateral surgical diseases of the kidneys depends upon the surgeon's ability to recognize prior to nephrectomy which is the diseased or more diseased kidney, and what is the functional capacity of the kidney that is to be left to carry on renal function, as well as upon his technical skill and the nature of the pathological process present. Tuberculous and pyogenic infections, unilateral and bilateral calculi, hydronephrosis, hypernephromas, and congenitally deficient or non-developed kidneys are the conditions in which the tests have proved of most value.

The urea, indigo carmine, methylene blue and diastase, cryoscopy, phloridzin, Alberran's polyuria tests, along with clinical studies and urinalysis of the separated urines, will all indicate which is the diseased or more diseased kidney. But in this class of cases the shortcomings of most of these tests are evident, since one kidney may be doing two or three times as much work as the opposite one and yet be incapable of assuming the additional work or of carrying on adequate work unaided. It may be doing the major part of the work, but only at the expense of its reserve power. But phthalein has prognostically one great advantage over other functional tests, in that it indicates the absolute as well as the relative value of each kidney, so that one knows not only which is the diseased or more diseased kidney, but the amount of work each is doing relative to the other, and what is yet of greater importance the amount of work for each relative to the normal, since this allows a prognosis concerning the capacity of the remaining kidney to carry on renal function. In double renal tuberculosis, in which for instance the amount of pus from each side is practically the same,⁵ the phthalein test may demonstrate that one kidney has a function far in excess of the other—in fact, so good a function that a successful nephrectomy can be done.

It must be admitted that depressed function, the result of inhibition due to ureteral catheterization, is sometimes encountered, in fact more frequently than we formerly believed. But in every case demanding ureteral catheterization a total renal determination should also be made through which any discrepancy can be readily detected and error be thereby avoided. Where leakage inhibition occurs reliance is placed upon urea percentage and diastase.

Of prognostic significance also is the development of increased functional capacity in the remaining kidney after a nephrectomy. In those cases in which determination of function has been made after an interval of a month after operation the capacity has not only been greater than that of the same kidney, but equal to or greater than that of the combined function of the two kidneys

⁵ Not infrequently in bilateral renal tuberculosis the more recently involved kidney secretes more pus than the other and only through functional tests can the true condition be recognized.

prior to surgical interference. The amount of increased function that will develop can of course not be predicted from functional studies, but the increase after nephrectomy can be determined from day to day and so aid in prognosis.

A perfectly normal urine in every respect except quantity may be excreted by a congenitally deficient type of kidney. Such a kidney may be capable of doing only one-fifth to one-tenth of the total work required. The literature furnishes numbers of instances of death following a nephrectomy owing to the presence of this unrecognized deficient kidney which has been left to do all the work. In the last four years in our experience four such cases have been encountered, and in the last case only the presence of a low phthalein from this kidney revealed its true nature and prevented the removal on the opposite side of a tuberculous kidney which had many times a greater function than this supposedly healthy kidney. Had the nephrectomy been performed the prognosis would have been extremely grave.

In certain cases, owing to malformation or stricture in the lower end of the ureters, and especially in bladder tuberculosis, it may be possible only to catheterize one ureter. When infection of the bladder exists, microscopic and chemical examination of the urine collected transvesically is obviously unreliable as indicating a healthy or diseased condition of the uncatheterized side. It is therefore necessary to use functional tests to determine the presence or absence of disease and the extent of the disease where it does exist. A prognosis may be safely made concerning the ability of any kidney to carry on the renal function alone even when catheterization of the ureter is impossible and where the urine has been collected through a diseased infected bladder, provided a catheter can be inserted into the other ureter.

The use of these tests should not be limited to renal surgery, since their routine employment would undoubtedly influence the surgeon's attitude in many instances.

UREMIA. Uremia is a clinical condition, a syndrome ill-defined, resulting from renal insufficiency from any cause. Its appearance is often sudden and unexpected, and its course is acute and severe, rapidly ending in death, or chronic, lasting through months. Through functional studies it is possible to ascertain that it is impending even when no indications whatever of its proximity are revealed by the clinical study. With a continued failure on the part of the kidney to excrete phthalein and lactose, etc., associated with the continuous marked and increasing accumulation of urea or total incoagulable nitrogen or low serum freezing-point, one is perfectly safe in predicting the early appearance of uremia regardless of the underlying pathological condition.

Uremia once present the clinical severity is not a safe criterion for prognosis. Apparently desperate conditions sometimes reveal

a fairly good renal function with an ultimate recovery, whereas very mild symptoms may be present until shortly before death. It always, however, indicates a serious condition, always calls for immediate therapeutic consideration, and always suggests a grave prognosis, but it does not always indicate a hopeless one.

It has already been intimated that identical functional pictures carry very different prognostic significance in different clinical and pathological associations. Extremely low functional capacity in chronic nephritis means death, whereas in obstruction in the lower urinary tract with urinary retention and back pressure the injury may be mostly functional, so that following appropriate treatment a fair or good capacity is again established. Nothing is more surprising than the rapidity and extent of the functional and clinical improvement. Whenever renal function markedly increases, surgical interference is much less liable to be followed by postoperative uremia, whereas in practically all cases with persistent low function it has followed operation used as a last resort, and death has ensued.

Markedly different clinical and functional conditions are encountered even in medical uremia. Some cases of mild uremia, with nausea, vomiting, and even stupor, show a phthalein output which is relatively high, 20 to 35 per cent. for two hours. This type is much more apt to be associated with cardiac or vascular changes, with edema frequently a prominent feature. The uremia symptoms may here be an expression of a different pathological condition than that encountered at other times, *e. g.*, edema of brain rather than a pure toxemia. These cases often improve and leave the hospital; if death supervenes, it is usually a cardiovascular affair and not a typical uremia.

Occasionally, with low excretory function (traces of phthalein) and marked cumulative phenomena, the patient will continue to live in a chronic uremia for a surprisingly long time. In several instances such a patient has lived for some months, and in one instance the patient lived a year. This patient is in a desperate condition but still continues to live with 20 per cent. phthalin for two hours and with a blood urea 2.5 gm. per hour. Vicarious activity probably varies markedly in different individuals, and though incapable of carrying on life alone for any length of time, it probably is a material aid in the maintenance of life when the kidneys are just verging on inadequacy. The balance is not long maintained, however, and death is continually imminent.

Uremia cannot occur without valuable evidence appearing as decreased excretory phenomena, but cumulative phenomena do not always arise. With Hohlweg we consider increased blood urea and rest-nitrogen indications of renal insufficiency and not of uremia.

THE PROGNOSTIC VALUE OF EACH TEST. The employment of one test alone does not always yield all the information desirable. When only one is used the phthalein test is undoubtedly the one of choice. When it reveals decreased renal capacity, one of the blood tests, urea, total incoagulable nitrogen, or cryoscopy, should be employed to determine the presence or absence of cumulative phenomena. These probably carry about the same significance.

Dye substances other than phthalein need not be employed prognostically, since they yield less quantitative and less reliable results and add nothing to prognosis.

The phthalein is the test for general use under all conditions. Its findings can be verified and its indications strengthened by the employment of selected tests in different conditions.

The iodide and salicylate tests are not of great prognostic value.

Lactose is unreliable, since its total suppression occurs in moderate lesions of a given type, but suppression in chronic nephritis indicates a severe lesion.

The urinary urea is of value only in relation to unilateral renal disease.

Phloridzin has a tendency to exaggerate the degree of functional injury, and hence is not of great value.

Salt. A marked tubular hyposthenuria carries much prognostic significance, otherwise the chlorides are of only slight prognostic value.

Water. A marked oliguria or anuria persisting is of significance.

Diastase may be tremendously depressed in moderate degrees of renal injury, in chronic passive congestion, while at other times it is not affected proportionate to the injury, hence it is not reliable for total capacity. In unilateral cases the diseased kidney is correctly indicated.

The value of total incoagulable nitrogen and of urea in the blood has been enhanced by the introduction of newer and more accurate methods by Folin and by Marshall. Increased concentration of these substances does not always occur in severe renal involvement, hence their normal concentration in the blood does not indicate normal kidneys. Their increase signifies renal injury, and the extent of the increase is of extreme value in determining the extent of the injury. They are not of value in determining the diseased kidney where only one is involved.

Cryoscopy occupies a similar position with about the same significance. A study of the combination of these three tests is needed in order to determine the extent of parallelism in their findings.

With cholesteremia we have had no experience, and with the Ambard-Constant not sufficient to justify an expression of an opinion.

IRON INFILTRATION IN THE FIXED AND WANDERING CELLS OF THE CENTRAL NERVOUS SYSTEM.

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IN a contribution to (a) iron infiltration in ganglion cells and (b) forced movement due to cellular degeneration of the cerebellum following rattlesnake poisoning,¹ I pointed out the existence of iron infiltration in the cortical ganglion cells both as an end result and as an intermediate process of the absorption of hemoglobin. The ganglion cells gave the biochemical tests for hemosiderin. The microchemical reactions in the large pyramidal cells in the cortex were striking and characteristic. In the Weigert-hematoxylin method the entire cell with its processes took a deep black stain. In thin sections this pigmentation seemed to consist of fine black granules; these black granules could be followed into the dendrites and produced an appearance of fragmentation. With the slow eosin stain the ganglion cells gave the same brilliant red reaction as did the red-blood corpuscles. With the potassium ferrocyanide and alcohol differentiation, the ganglion cell as a whole gave a diffuse blue reaction without, however, the granular arrangement of the hematoxylin stained cell. This microchemical reaction in the ganglion cells was not obtained throughout the entire cortex, but only in the neighborhood of the diseased vessels.

Weber² has described iron infiltration in the cortical ganglion cell with similar changes to those here noted, but no other contribution, so far as I have been able to determine, has been made to this subject. This condition must indeed be a rare one, as I have noted it, as a complete reaction, only in the case above noted, reported by me. It is not a constant reaction in hemorrhage into the cortical tissues. I have looked for it in a large number of brains showing cortical hemorrhage, with degeneration of the red cells in various stages, but have not been able to find it. In a series of experiments on young puppies an artificial thrombosis of the venous sinuses was produced in an attempt to simulate the venous capillary hemorrhage observed in some cases of the cerebral palsies of childhood. Capillary hemorrhages in the tissues were produced, but no end reaction of hemosiderin was noted. What might be considered an intermediate reaction was the rule. Cells took a deep black stain with hematoxylin and a deep red stain with eosin, but no blue reaction with potassium ferrocyanide was obtained. The results of this series of experiments were inconclusive in

¹ Contributions from the William Pepper Laboratory of Clinical Medicine, 1900, vol. i.

² Monats. f. Psychiat. u. Neurol., 1898, No. 3.

demonstrating a structural change in the ganglion cell as a result of long-standing venous stasis or thrombosis occurring at the time of delivery. The experiments have not yet been completed, but so far as they have been carried, an artificial infiltration of hemosiderin in the ganglion cells has not been produced. In line with this work a careful investigation of ganglion cells was made in the brain from a patient who suffered from an extensive hemorrhagic encephalitis in the cortex. The iron reaction was not demonstrated in the cortical ganglion cells in this case, but was obtained in a striking cell reaction in the plasma-like cells of the pia arachnoid and in the elastic coats of the smaller cortical arteries. The case was as follows:

The patient, R. L., a white male, was admitted to the hospital, June 1, 1910 in a semi-unconscious condition, in which he remained for four days. On admission his neck was rigid, his pupils contracted and his reflexes exaggerated, and since the stuporous condition had been present, any attempt to move his neck or bend his back caused him to cry out as if from pain. Pressure upon the muscles also caused him pain. He had incontinence since his admission. Owing to the noise he made during any attempt to examine his heart and lungs an accurate knowledge of their condition could not be ascertained. There was, however, apparently no valvular lesions of the heart. In the left lung many dry rales could be heard in front. The patient had an old, depressed fracture near the Rolandic area on the left side. There was a large discolored area over the right temporal region; and just below the left deltoid muscle, on the outer side of the arm, was a large bruise. He had been operated upon shortly before coming into the hospital for a tuberculous fistula in ano, which was still unhealed. His wife later stated that he had been operated upon for fracture of the skull in September, 1908, which explained the depression.

On June 25, an examination of the eyes showed the eye-grounds to be normal, though the optic nerves were very small. A lumbar puncture revealed nothing abnormal macroscopically or microscopically, but a Noguchi (Butyric acid) test was positive. The urine had a specific gravity of 1026, and contained a trace of albumin; the microscope revealed granular casts, triple phosphates, and amorphous urates. The temperature was normal except for a slight rise during the fortnight preceding his death. The patient died July 25.

The autopsy on July 26 permitted the following diagnosis: Dilatation of the left ventricle; fibroid myocarditis; congestion and edema of the lungs; an old fracture of the skull; a chronic internal hemorrhagic pachymeningitis. The general postmortem examination showed nothing more than the above diagnoses suggest. The man was fairly well-nourished; the lungs were free and crepitated throughout, but contained frothy bloody fluid, while the pleural

cavities were empty. The heart was flabby, with the muscle pale in color, but no lesion was found in the valves, and the coronary arteries were smooth. The papillary muscles were slightly fibroid at the tips, and the aorta showed a few yellowish patches. The liver contained an excess of blood, and the spleen was large and soft. The pancreas, adrenals, ureters, and bladder were normal. The kidneys showed no noteworthy change. There was no gross lesion of the intestines, but these with the stomach, which presented a dark reddish mucosa, were distended. In the abdominal aorta were a few calcareous patches.

The skull showed a fracture partly linear in type, extending from the right posterior fossa just behind the foramen diagonally across the median line to the left fossa, and running superiorly and anteriorly close to the juncture of the parietal and temporal bones and terminating anteriorly at the base of the skull, just posterior to the orbital plate of the frontal bone on the left side. There were two small circular deficiencies in the frontal bone of the left side near the median line.

The brain showed slight excess of fluid. The inner surface of the dura, over practically the entire hemisphere, but especially posteriorly and superiorly, was thickened and darkened in color. At points the thickening appeared to be due to fibrin. At other places it appeared to be newly formed tissue. Posteriorly the superior surface of the brain showed a distinct depression underneath the thickest portion of the dura. The cord presented no gross lesions.

The gross examination of the brain, after hardening, showed at the base an advanced grade of arteriosclerosis of all the vessels composing the circle of Willis. There was a slight trace of chronic leptomenigitis over the base of the frontal lobes, and there were evidently adhesions between this and the dura of the base, which were torn away when the brain was removed. There was a yellowish pigmentation of the pia arachnoid over the base of the frontal lobe on the left side and the tip of the left temporosphenoidal lobe. Pons and medulla were normal. There was an extensive hemorrhagic internal pachymeningitis involving the dura over the convexity of the left hemisphere. On this side of the brain the pia arachnoid was adherent to the dura over the anterior half of the frontal lobe. The pia arachnoid as far back as the midparietal area had a yellowish red appearance, as if infiltrated with an old transformed blood pigment. Here and there throughout the frontal lobe, and more particularly where the pia arachnoid was adherent to the dura, the cortex was friable and softened as if from a recent thrombotic lesion. Sections of the cortex showed that the reddish-yellow pigmentation extended into the gray corticle matter, while the underlying white matter had the appearance of yellow softening. The dura over the right hemisphere was the seat of a localized pachymeningitis (6 cm. long by 3 cm. broad) situated over the

inferior parietal area. The internal surface of the dura was perfectly normal, both in color and texture. The external surface of the dura was roughened, indurated, and of an orange-brown to black color. Section of this area showed this condition for the most part to be extradural. The pia arachnoid on the right side was normal in texture and color, as was also the cortex. Transverse section of the brain showed nothing abnormal.

Microscopic Examination of the Brain Cortex. The left cerebral cortex showed here and there throughout the frontal area capillary hemorrhages, both old and relatively recent. The cortex in sections taken from the frontal lobe showed necrotic areas extending from the surface into the subcortical tissue in the form of pyramids. At the apices of these pyramidal areas of degeneration there was proliferation or neuroglia, while the body of the pyramids was composed of partially degenerated cortical substance and partially organized cortical scar tissue. New-formed capillaries were scattered throughout this area, and here and there capillary hemorrhages were present. A large number of a vesicular type of cell, containing an orange-brown pigment, was scattered through the areas of degeneration.

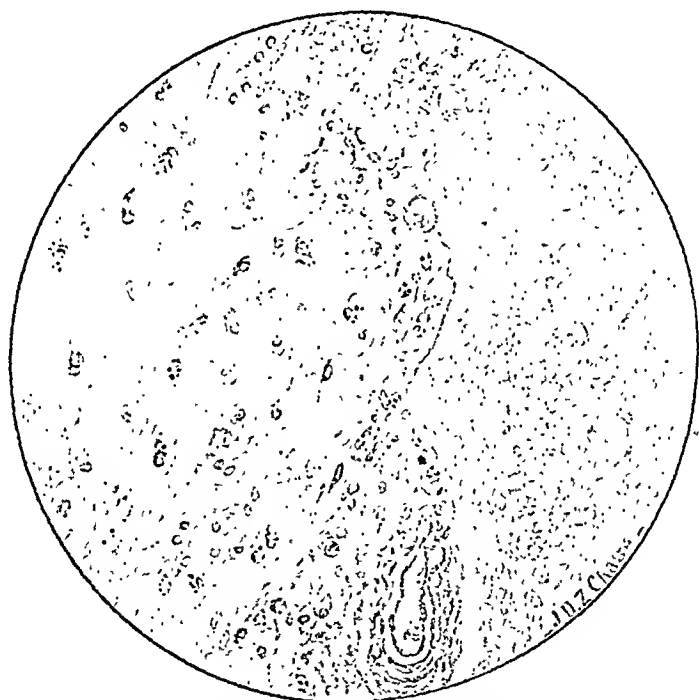
The dura mater over the left side of the brain was composed of laminæ of fibrous tissue, containing a great number of cells, mostly with connective-tissue nuclei, and containing pigment varying in color from light yellow to black. On the inner surface there was a layer of pseudomembrane, composed of trabeculæ of connective tissue, new-formed capillaries, and a great number of red-blood corpuscles. The connective-tissue cells contained yellow and black pigment.

Throughout the motor cortex on the left side there was a proliferation of neuroglia cells in the tangential and subtangential layers. The pyramidal cells showed a mild grade of chromatolysis, and appeared to be fewer in number than in the normal cortex. The left parietal and occipital areas were normal in structure. The cortical tissues of the right side revealed no abnormal change.

The pia arachnoid of the frontal and motor area of the left side showed a proliferation of the connective-tissue trabeculæ with an infiltration of red-blood cells, in various stages of degeneration into the interstices. Scattered through the arachnoidal spaces were found a great number of cells of a large vesicular type, filled with pigment varying in color from a light yellow to an orange-brown. The relative number of these cells in the sections depended upon the degrees of hemorrhagic infiltration in the meninges and neighboring tissues.

All the tissues showing this condition were stained for hemosiderin. The Berlin-blue reaction was not obtained in any of the cortical cells. A well-defined, clear-cut, blue reaction was obtained, however, in many of the vesicular type of cells in the pia arachnoid.

The elastic tissue in the small arteries of the pia arachnoid and superficial areas of the cortex took the same clear-cut, blue color as did the plasma cells above mentioned. None of the other tissues gave this reaction. Sections of the bloodvessels gave a microscopic picture, very much as that seen in the sections stained with a selective elastic stain. While the cortical ganglion cells did not give the stain reaction for hemosiderin in the sections stained with iron hematoxylin, both the neuroglial nuclei and the partially degenerated cortical ganglion cells in the neighborhood of the pyramidal areas of necrosis, gave a jet-black reaction, which I have already pointed out in a previous contribution to this subject may be considered as a partial or transitional stage between hemoglobin and hemosiderin.



Section through cortex and pia arachnoid. The small cells with hard granules gave the typical hemosiderin reaction. The small vessels also presented the Berlin-blue reaction.

Sections from the spinal cord showed a degeneration in the cross-pyramidal tract of the right side.

The area of external pachymeningitis on the right side was found, under the microscope, to be composed of (a) a normal dura somewhat thickened, and (b) external to this a thick layer composed of fibrous tissue, but relatively looser in consistence than that of the normal dura, containing a large number of connective-tissue nuclei and here and there large areas in which red-staining nuclei the size of red-blood corpuscles, but irregular shape, were found arranged in columns and nests. Connective-tissue nuclei and large

irregular cells scattered here and there contained masses of dark pigment having the appearance of melanin.

The biochemical microscopic reactions here noted threw some light on the minor changes in the nerve cells, leading to a disturbance of function, without apparent structural change. The partial reactions to iron infiltration shown in the ganglion cells, together with the complete reaction noted in the arachnoidal free cell, and in the coats of the capillary vessels were evidently only temporary in nature. These changes may entirely disappear, and studies of these tissues in after life would leave us without any evidence of these previous pathological lesions. In a complete stage of iron infiltration in the cortical ganglion cells, complete chromatolysis with disintegration of the cell occurs. In the minor grades of iron infiltration, relatively little structural change is noted in the cell. Granted such a transitory process, extensive disturbance of the function may result without leaving any changes evident in the histological picture. In cases of mental retardation, high-grade imbecility, etc., the brain structure not infrequently presents a normal histological picture. There is no reason, in this group of cases, why the functional activity of the brain cells should be subnormal. In conditions of prolonged passive congestion at birth, and more particularly in those cases where the microscopic examination of the newborn children, dying at or shortly after birth, reveals an osmotic extravasation of red-blood cells in the tissues, a medium grade of iron infiltration may well have taken place, leaving the brain structure normal, but with deficient functional power.

The meaning of the hemosiderin reaction in the elastic coats of the capillary vessels is not altogether clear. None of the other coats of the vessels gave this reaction. It is evidently a selective reaction, due to some changes in the elastic fibres. It was not present in the larger vessels within the area of blood extravasation and degenerating blood cells.

The extensive vascular changes noted in this case are of considerable interest from the standpoint of legal medicine. As a result of traumatism of the head, with a linear fracture, the following series of changes are presented: Extensive cerebral necrosis with hemorrhagic extravasation into the cortex on the side of the lesion, internal hemorrhagic pachymeningitis on the opposite side, together with an area of external hemorrhagic pachymeningitis on the posterior part of the dura on the side opposite to the bone lesion. There is a history of the excessive use of alcohol. How far are these changes due to the original trauma? It has been held by experts in court that concussion with a prolonged period of unconsciousness, without evidence of focal lesion or lesions, produces disturbances of the physical or nervous health of the individual, from which he practically never recovers. The lack of

resistance to stress and strain in such cases, a matter of clinical observation, not only in medicolegal cases but also in cases without a cause for legal action is probably due to relatively minor changes in the cerebrovascular system as compared to those here noted.

In the history of this case, it is shown that the patient apparently recovered from the cerebral injury after the operation. A succession of vascular accidents beginning with the cerebral injury and possibly influenced by the excessive use of alcohol took place, leading finally to his death. It is reasonable to suppose that these changes would not have taken place in the absence of any such injury. Certainly, the exact nature of the changes was determined by the extensive laceration of the brain tissue incidental to the original brain injury. Extravasating hemorrhage into the pia arachnoid is a relatively rare pathological phenomenon. I have seen it in one other case affecting approximately the same distribution in the brain in a case of locomotor ataxia.

The necrosis of the cortical and subcortical tissue is difficult to explain. It is possible that the inflammatory adhesions of the pia arachnoid to the dura produced partial or complete obstruction of the cortical capillary or both the capillary and the cortical venous circulation. The pyramidal shaped areas would be more in favor of a subcortical capillary destruction.

A PRACTICAL APPARATUS FOR THE PRODUCTION OF THERAPEUTIC PNEUMOTHORAX: WITH SOME NOTES ON THE MODUS OPERANDI, INDICATIONS, AND CONTRA-INDICATIONS.¹

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IN presenting this new apparatus, originally the Forlanini apparatus, which was modified by Saugman, again by Muralt and Nebel, and then upon my suggestion made by the Kny-Scheerer Company in a little more substantial form, more easy to transport, more clearly graduated, and with glass tubes inserted in the rubber hose connecting the apparatus with the thoracic cavity, I do not wish to claim any credit for bringing out what I believe to be a very superior apparatus. The credit is due to the original inventors, Professors Forlanini and Saugman, and also to the Kny-Scheerer Company, who, as above stated, have made the apparatus compact, safe, and transportable.

¹ Read by invitation before the meeting of the Association of Physicians attending the Tuberculosis Clinics of New York City, October 8, 1913.

Those who have had experience heretofore with the Forlanini apparatus now on the market, will appreciate the difference. Shipped from a distance, the apparatus usually arrived with the glass tube broken and the gas containers unsupported, and if not broken, liable to break at the slightest jar.

Among the modifications which I have incorporated in this new apparatus, besides the better support of the gas receptacles and stop-cocks, is a manometric scale. In the older apparatus it consisted of a narrow strip of paper, with no light background, which made the reading of the oscillation exceedingly difficult. The scale in the new apparatus is made of a broad strip of milk glass, which at the same time serves as a background to make the reading indicated by the colored liquid more easy.

The manometric scale is divided into 50 cm., 25 cm. above and 24 cm. below zero, indicating respectively negative and positive pressure. To make the reading as easy as possible, every division has a number, and the 5, 10, 15, 20, and 25 are cut in larger and heavier figures. The old apparatus does not indicate all numbers, only 5, 10, 15, etc.

To increase the pressure, the rubber bulb in this apparatus is smaller than in the one heretofore on the market; this is for the purpose of better control when it is desired to use a little more pressure in the flow of nitrogen. The reason for having two intervening glass tubes in the rubber hose connecting the pleural cavity with the apparatus is to enable the operator to see at once if the needle is drawing fluid serum, pus, or blood. It was a peculiar accident which made me see the necessity of this modification in the connecting hose. Prior to practising the pneumothorax operation myself, I decided to see as many experts operate as possible. For this purpose I had visited a colleague in a neighboring State, who operated on a case in my presence. When the needle was inserted, the manometer rose and fell to a considerable degree. My colleague, who has had a large experience in artificial pneumothorax, stated that he could not account for the behavior of the manometer. He turned on the gas-cock, but no gas would flow. He finally gave up the operation and withdrew the needle, and the patient left the table neither better nor worse for the experiment. When the doctor tried to clean the apparatus and needle, he discovered the connecting tube to be full of pus. This explained the peculiar behavior of the manometer, and gave me the inspiration for the employment of the intervening glass tube.

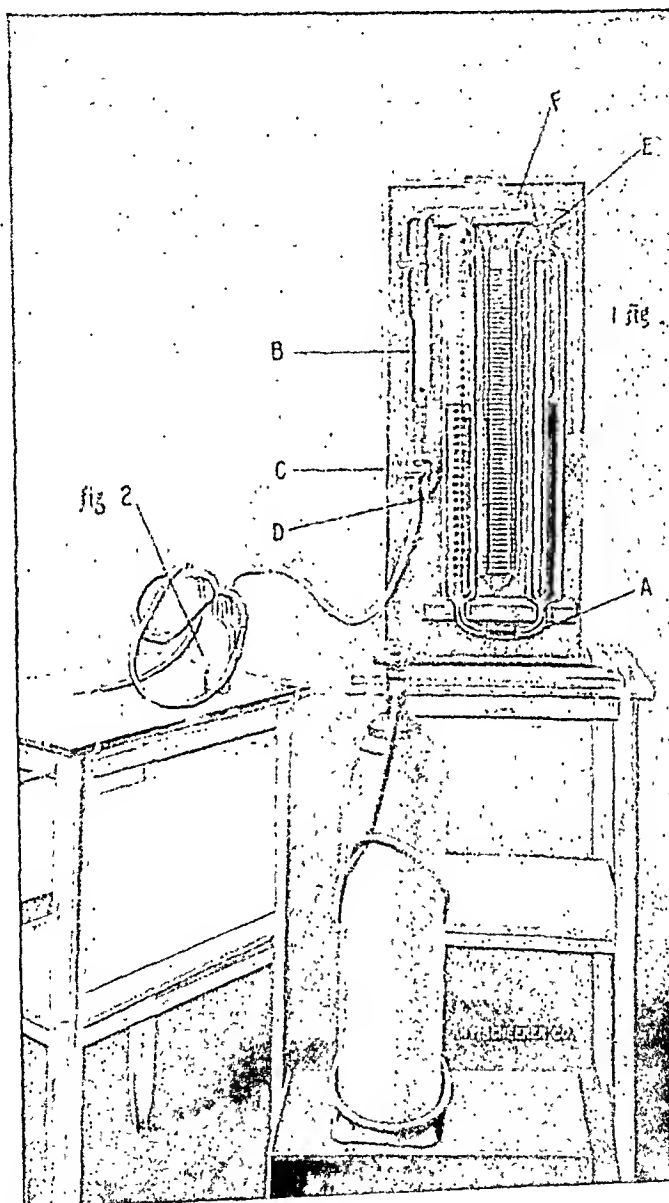
For the benefit of those not familiar with the apparatus, the following is a summary of its workings: (See illustration.)

The apparatus, in a general way, consists of two glass tubes $24\frac{1}{2}$ inches high and about 2 inches in diameter. These two tubes are joined by means of a rubber hose under the base A.

The tube at the left is graduated to 1000 c.e.

The two receptacles are filled with water up to 500 c.c.

The graduated tube to the left hand is filled from the tank with the gas to be introduced into the pleural cavity by the weight of the water in the tube, or by additional pressure, the latter being obtained from a double rubber bulb. The flow of gas into the



intra-pleural space is slow but steady. The graduated tube is connected with a glass tube containing sterilized gauze *B*, serving as a filter. It has a ground-glass stopper, which can be removed for the renewal of gauze or cotton.

The filter communicates with a two-way diagonal-passage

glass stopcock *C*. Stop-cock *C*, when turned with the arrow downward, connects the instrument to the gas supply tank (nitrogen or oxygen) by means of a rubber tube. The stop-cock, in the same position, serves for the introduction of the gas into the intrapleural cavity.

When stop-cock *C* is reversed, that is, with the arrow pointing upward, it is connected to the manometer by a thinner glass tube, mounted between the large glass tubes, thus showing the oscillation when the needle is in the intrapleural cavity.

When the arrow of the by-pass stop-cock *D* is pointing horizontally it permits the manometric reading, showing the degree of oscillation while the gas is still flowing provided, of course, that the arrow of stop-cock *C* is turned downward.

When filling the instrument with gas, the rubber hose from the tank should be connected to the outlet below stop-cock *C*. Stop-cock *D* should stand vertically; the arrow on stop-cock *C* should point downward; stop-cock *E*, on the top of the non-graduated tube, should be turned horizontally to the left. When the flow of gas is no longer desired, stop-cock *C* should be turned so that the arrow points upward. If additional pressure is desired, stop-cock *E* must be turned with arrow pointing upward.

Funnel *F* connected with the manometer serves for the filling of the manometer tube to zero with an alcoholic solution of methylene blue.

The illustration shows a transportable tank of nitrogen containing 25 cubic feet, which is equal to 175 gallons, or 700 liters, under the pressure of 1800 lbs., per square inch. The same size tank, containing oxygen under similar pressure, can also be procured. While nitrogen may be obtained more cheaply from the air or with the aid of pyrogallie acid, the use of the tank will be found more convenient and simple.

Owing to the high pressure under which nitrogen or oxygen is held in the tank, great care should be exercised that the liquid is not blown out of the glass tube when filling the apparatus. The surest way is to have an intervening rubber bag into which the gas flows first, and from which it can gradually be pressed into the receptacle of the apparatus; but with care the flow of gas from the tank can be regulated so as to avoid accidents. The flow should always be regulated prior to attaching the receptacle to the apparatus.

In addition to this new apparatus, the illustration shows a device which will eliminate at least one of the unpleasant features which occasionally attend primary as well as subsequent operations for artificial pneumothorax. The distress which the patient sometimes feels, manifesting itself in anxiety, intense dyspnea or cardiac pains, and which is due to the expansion of the nitrogen which has been injected at the temperature of the room. The much higher

temperature of the thoracic cavity causes the gas to expand and thus increase considerably in volume. To eliminate the possibility of this accident, a coil of metal tubing is suspended over an alcohol lamp (see illustration), through which tubing the nitrogen gas is passed before it enters the pleuritic cavity. Pneumonia has been said to have been produced by the inhalation of cold oxygen, hence it is suggested that when oxygen is chosen as the gas to be injected for the production of artificial pneumothorax, it should be passed through a heated coil of metal tubing, after the alcohol flame has been extinguished, to avoid any possibility of explosion.

Robinson and Floyd state that the warming of the nitrogen will materially aid in preventing a "pleural reflex."

As to the manner of producing artificial or therapeutic pneumothorax, all antiseptic precautions, sterilizing of hands, needles, and field of operation, should be rigorously adhered to. While the operation is seemingly slight and many times accomplished without any accident whatsoever, serious and even fatal accidents have happened. Therefore, the operation should be performed either in the home of the patient or in the hospital, but never in the physician's office.

Furthermore, one should not undertake to treat a patient by compression of the lungs unless the latter is informed that it will take a long time and probably many inflations before a successful compression is obtained. He should also be told that the operation is not always successful.

To avoid accidents from shock, infection, or even temporary discomfort, the patient should be prepared by having his bowels moved. Prior to the inflation a quarter of a grain of morphine should be injected. The skin should be rendered aseptic by tincture of iodine. A local anesthesia of the skin should be produced by ethyl chloride, prior to the insertion of the needle for the injection of novocain, to anesthize the muscular layers of the thorax.

Before beginning, the apparatus should be tested to see that it is working properly. Since it is not always possible to locate a point free from pleuritic adhesion, several punctures may be necessary before the manometer indicates free oscillation, which means that the needle is in the interpleural space. Large needles which require a preliminary incision into the skin and thoracic muscles may lead to septic infection, particularly when several incisions become necessary. A finer needle is not likely to do serious damage, even if it does enter the lung. The regions which are apt to be more frequently free from pleuritic adhesions are along the axillary lines. The Kny-Seheerer Company have manufactured for me a moderately fine needle, which by means of a cap can be easily attached to the rubber hose connecting with the manometer or gas receptacle.

The patient should be placed on his side, with the arms up,

so as to widen the intercostal space. The needle is then slowly inserted through the skin and muscular layer in such place as percussion and auscultation had showed a seeming freedom from adhesion. When the needle penetrates the parietal pleura, free from adhesion, a peculiar resistance is felt, which might be likened to the passing of a needle through stretched parchment. When the manometer indicates a negative pressure, with free oscillation the gas is allowed to flow.

As an initial inflation, perhaps not more than 500 c.c. should be injected, except when the injection is made for uncontrollable hemorrhage, then larger quantities may be indicated.

To avoid gas embolism, it is advisable to begin with an inflation of 50 to 100 c.c. of oxygen. In cases of uncontrollable hemorrhages the more oxygen injected the better the patient feels from the operation. Dr. Mary E. Lapham,² who has had a large experience with artificial pneumothorax, recommends the substitution of oxygen for nitrogen whenever the introduction of the latter gas causes dyspnea and cardiac distress.

As stated above, it is best to inject small quantities of gas at the beginning (about 500 c.c.) This, as a rule, suffices to give the desired relief, reduces temperature, and influences cough and expectoration favorably. Robinson and Floyd, however, give as a maximum for the first injection 1000 c.c., and Bonniger³ as much as 2000 c.c. in a strong man and 1600 c.c. in a woman. Concerning this, King and Mills⁴ say: "These larger quantities seem to us unnecessarily heroic, and not altogether devoid of embarrassing sequela if not of danger." In regard to the subsequent injections, the latter say: "Subsequent inflations had best be made at intervals of not more than a few days, until the manometer readings are neutral or slightly positive and the x-rays show as complete a lung compression as is possible. After this is accomplished, the intervals between the injections are governed by symptoms, especially the amount and character of the sputum, temperature, etc., and by the x-ray. If atmospheric air is used, the intervals will necessarily be shorter than when nitrogen is employed."

Atmospheric air should never be used unless it is passed through the filter referred to in the above description of the apparatus and rendered sterile.

Before referring to the indications and contra-indications, it may be stated that sometimes the most careful injection is followed by an immediate surgical emphysema. When the beginning of such a complication arises, the emphysematous area should be encircled by a rubber bandage, which usually suffices to control

² Artificial Pneumothorax, New York Med. Journ., March 22, 1913.

³ Berl. klin. Woch., August 26, 1912.

⁴ Therapeutic Artificial Pneumothorax, AMER. JOUR. MED. SCI., September, 1913.

the condition. Pleuritic effusion may occur later on and should be treated in the usual way. Collapse caused by pleural reflex, intense dyspnea, or hemorrhage, should be treated with injections of morphine, caffeine, nitroglycerin, and locally with spirits of ammonia, whisky, hot-water bags, and ice-bags.

The cases which justify the operation of therapeutic pneumothorax although discussed before⁵ may bear repeating. (1) Artificial pneumothorax is indicated first in all such cases as have not improved under ordinary hygienic, dietetic, climatic, and symptomatic treatment. Such cases are, as a rule, moderately or far advanced.

(2) It is indicated also in those earlier cases in which there is no improvement because of mixed infection or lack of recuperating powers, or when for other often inexplicable causes the condition remains stationary or the progress toward improvement is particularly slow.

(3) In all rapidly progressing cases, whether they are treated in institutions or at home, and in whatever climate.

(4) It is indicated for all patients of the moderately or far advanced type, within or outside of institutions, who are discontented, feel that not enough has been done for them, and who are desirous to have artificial pneumothorax tried.

(5) It is indicated in uncontrollable hemorrhage or chronic sanguineous expectoration.

(6) In that group of cases, which King describes as uncomplicated unilateral phthisis, with slow or subacute course, regardless of the degree of lesion, but with such pleuritic adhesion as may be removed by artificial pneumothorax.

(7) In cases of bronchiectasis, when climatic, hygienic, and the ordinary symptomatic treatment fails, it is justifiable to try the injection of nitrogen gas, with a view of producing artificial pneumothorax. There are a few cases on record where this means has been successful.

Bilateral involvement, if one lung is more involved than the other, is not a contra-indication to the production of artificial pneumothorax. Those who see many tuberculous cases, both in private and hospital practice, will admit that tuberculosis limited to one side is rare in patients who have had the disease for any length of time. In my service at the Riverside Hospital Sanatorium, where from 300 to 400 cases are treated in the second and third stages of the disease, it is doubtful if there is one in whom the tuberculous lesion is confined to one side. Most of the cases operated on in sanatoria and hospitals have had bilateral lesions, and a fair number have shown gratifying results.

Interesting and paradoxical as it may seem, all clinicians doing artificial pneumothorax work have frequently noticed that in spite of the increased activity of the less involved portion of the

⁵ Knopf and Lapham, Artificial Pneumothorax, New York, Med. Journ., March 22, 1913.

lung, as a result of compression of the other side a concomitant improvement has resulted in this non-treated part of the pulmonary lesion.

Casts and albuminuria are not necessarily a contra-indication, but, of course, one must be guided by the general condition of the patient. When the lesion of the less affected side is a basal one, some authorities consider this a contra-indication. In the opinion of Dr. Lapham, this condition is not an absolute contra-indication, and the production of artificial pneumothorax is permissible because of the relief which it gives to the patient.

There are of course decided contra-indications to the production of artificial pneumothorax:

1. An extensive involvement of both lungs.
2. When there is so much cavitation in the affected lung that there is danger of the needle entering a cavity.
3. Dry pleurisy or pleurisy with effusion.
4. Myocarditis, other serious cardiac complications, or serious renal complications.
5. Pulmonary tuberculosis complicated by any constitutional disease which in itself is sufficient to inhibit all possible chances of recovery.
6. When there is an ascites or a distention of the abdominal cavity due to gases in the stomach or intestines, artificial pneumothorax must not be produced until this condition is remedied, otherwise a serious dyspneic condition and heart complications might ensue.
7. When the patient, in no matter what stage of the disease, is too apprehensive and strongly objects to the performance of the operation, it should not be resorted to.
8. Finally I would wish to say artificial pneumothorax is contra-indicated in early and favorable cases.

There are a few clinicians who, because of their success in advanced cases, recommend its use in early unilateral lesions. My experience and knowledge up to this date make me consider an early lesion of pulmonary tuberculosis a contra-indication and not an indication for the performance of artificial pneumothorax. Such early uncomplicated cases, with relatively little involvement, should be treated by the well-tried sanatorium methods in special institutions or at home. Artificial pneumothorax can as yet only be classified as a valuable therapeutic means in a limited number of cases of pulmonary tuberculosis, but it cannot be considered the treatment of this disease in all stages.

TONSILLAR INFECTION:

A PRELIMINARY REPORT CONCERNING THE PASSAGE OF ANTHRAX
BACILLI THROUGH THE TONSILLAR TISSUES AS DETER-
MINED BY EXPERIMENTAL RESEARCH.

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THE determination of the importance of the tonsils as a gateway for cryptogenic infections is one of the most difficult problems in the domain of the laryngologist. Notwithstanding certain sporadic outbursts of conservatism, both from specialists of repute and from those who by striking fire desire to gain fame, the progressive clinicians are becoming more and more convinced that the tonsillar masses of the throat are responsible for a large number of general systemic infections. It takes a long time, careful observation, and many reconsiderations to arrive at the truth of a difficult subject through clinical study alone, hence the necessity of recourse to animal experimentation. The disadvantages, however, of this method are manifold, especially so when we come to study tonsillar tissues. Practically the only available animal which has a tonsillar structure sufficiently large and easy of approach for study is the hog, but unfortunately the hog is one of the most resistant of animals to the invasion of microorganisms. There are, however, certain diseases to which this animal is subject, and it was thought that by using the specific organism of one of these diseases the importance of the tonsillar tissues as a gateway of infection might be studied experimentally.

In 1904 I published the results of a series of experiments on tuberculosis. In those experiments I confirmed certain results, previously obtained by Ravenel, showing that the tonsils of the hog are readily inoculated without trauma by simply bringing tubercle bacilli in contact with the mouths of the crypts. Ravenel found that the tonsils were always infected where tubercle bacilli were present in the food. In my own work I rubbed a swab saturated with an emulsion of tubercle bacilli over the tonsils and always obtained a successful inoculation. I might state that in no instance was any other portion of the pharyngeal mucosa involved. As far as the tuberculosis is concerned, these results have been verified by the clinical and postmortem examinations of human tuberculous subjects. It is safe to say that at least 90 per cent. of all people dying from pulmonary tuberculosis show

secondary involvement of the tonsils. Also, as shown by a collective study, the average proportion of primary tuberculosis of the tonsils in children is from 4 to 5 per cent. of all tonsils removed by operation.

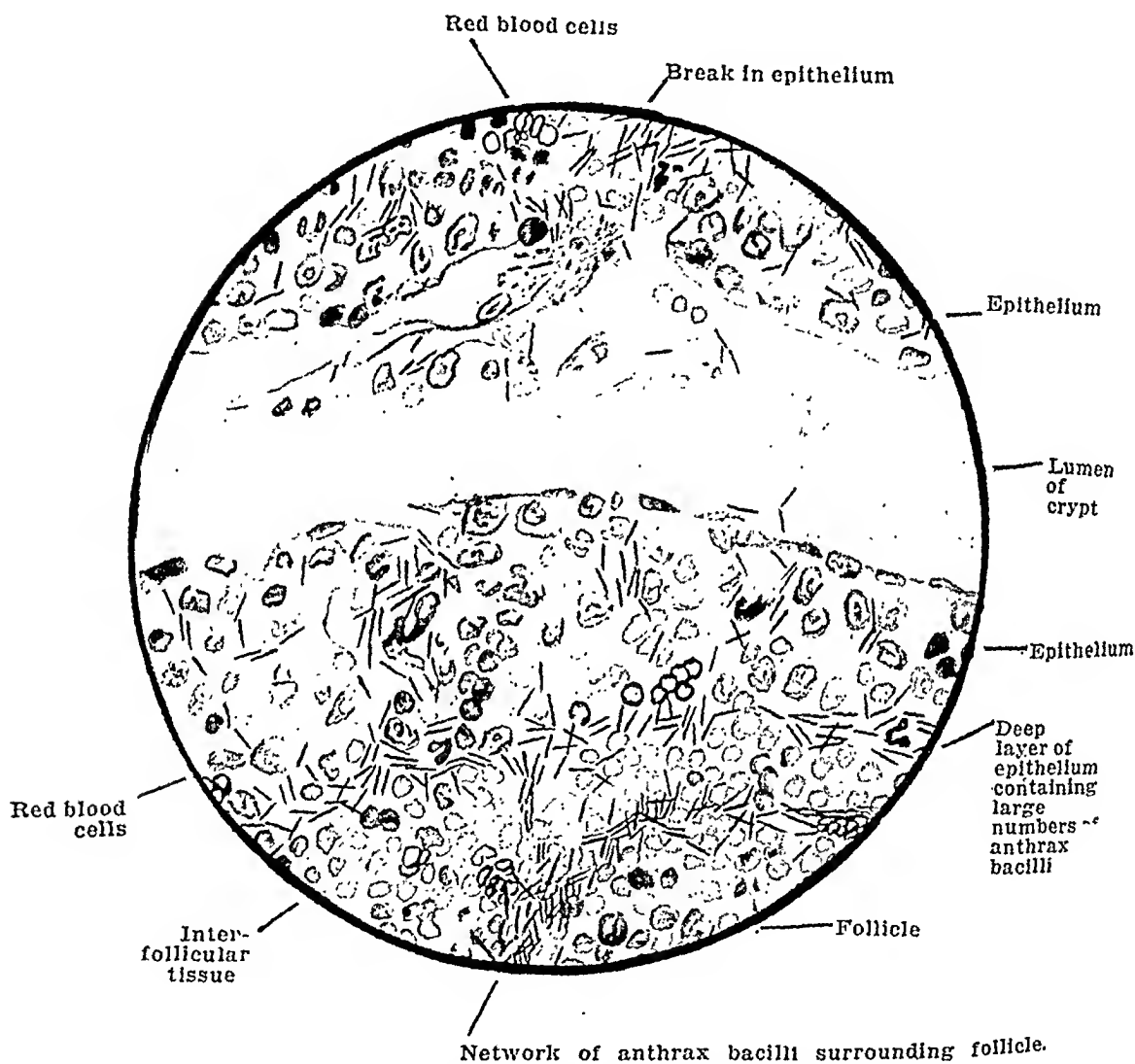
These results, however, do not warrant the assumption that the tonsils are open to a similar invasion from other organisms, and especially from those causing acute infections. In our study of tonsillar invasion we must remember that only pathogenic bacteria can be considered, and in experimentation it is frequently found that bacteria pathogenic to man are not so to animals. For instance, a strain of streptococci obtained from a case of acute rheumatic arthritis was injected directly into the blood of a hog. This was done to find out whether lesions similar to those in man could be reproduced in a hog, and if such lesions developed an effort was to be made to determine the possibility of the tonsils acting as a portal of entry. Unfortunately for the experiments, the inoculated hog flourished and grew fat under doses that would have proved fatal to almost any other animal. It was, therefore, necessary to choose an organism of known pathogenicity to the hog. The two which seemed most likely to afford results were the anthrax bacillus and the bacillus of hog erysipelas. The former was easily obtained and possessed certain advantages, namely, its ready staining in tissues and its easy culture on ordinary media, and was therefore selected for the work outlined in this paper.

Anthrax is a contagious disease commonly found among the domestic animals, frequently appearing in epidemics. It occurs sporadically among hogs, but never in the epidemic form, and it has been shown that certain breeds of hogs are more resistant to the invasion than are other species; also the adult animal is more resistant than the young, and it is probable that individuals show varying degrees of susceptibility. Among hogs pharyngeal anthrax is by far the most frequent variety. Occasionally the source of infection is through the intestine and then the symptoms correspond to inflammation of these organs. The course of the disease is very rapid, and the animals generally die in from one to two days, though sometimes they will live several days or a week. In pharyngeal anthrax the portal of entrance is always the tonsils. It has been reported that the base of the tongue and the pharynx are occasionally the atrium of infection, but there is no proof that such is ever the case.

EXPERIMENTS. The first two hogs used in these experiments had previously been inoculated into an ear vein with a strain of streptococci, taken from a case of acute articular rheumatism. This was done to determine the susceptibility of the hog to rheumatic infection. There was, however, absolutely no reaction either local or general.

Hog No. 1. Animal weighed about fifty pounds, and was in good condition.

March 14. The surface of the tonsils, especially the right, was rubbed over with a twenty-four hour culture of virulent anthrax bacilli. (The culture had not been previously emulsified.)



Penetration of anthrax bacilli through the living epithelium of a tonsillar crypt.

March 15. Animal was killed with chloroform. Cultures were made from the prescapular, submaxillary, subparotid, and retropharyngeal lymph nodes, also from cut surfaces of each tonsil. The tonsils were removed and kept for histological study. Except for a slight congestion of a small part of the right tonsil, there were no gross lesions.

All the cultures from the lymph nodes, after having been incu-

bated for two days, remained sterile. Cultures from the tonsils showed staphylococci and other organisms, but no anthrax.

Histological examination of the tonsils showed normal tonsil structure, except that a few of the crypts possessed an excess of polymorphonuclear leukocytes. In a few crypts staphylococci were found, but no anthrax bacilli could be seen anywhere.

Comment. This was a negative experiment, and a possible explanation of the failure of inoculation was that the bacilli were not first sufficiently separated before they were applied to the surface of the tonsil.

Hog No. 2. Animal weighed about fifty pounds, and was in good condition.

March 18. Tonsils were swabbed with an emulsion of anthrax bacilli, most of it being rubbed into the right tonsil.

March 20. Animal was killed with chloroform. Cultures were made on agar from both tonsils, the left subparotid lymph node, the left retropharyngeal lymph node, the left prescapular lymph node, the right retropharyngeal lymph node, the bronchial lymph nodes, the lung, the spleen, the liver, and the kidney. Bouillon cultures were made from the blood, the stomach, the large intestine, and the small intestine.

The tonsils were flecked with fibropurulent exudate, apparently coming from the mouths of the crypts. On the left tonsil there was a coalesced area involving about one-quarter of the tonsillar surface. The tonsils were slightly swollen and protruding on the surface. There was no distinct congestion to be seen from surface examination, but on section there were definite inflammatory striæ running through the parenchyma from the surface toward the base. A few small abscesses were found in the tonsillar substance.

The *cervical lymph nodes* were normal.

The *lung* showed scattered throughout its substance a number of circumscribed, congested, and slightly edematous atelectatic areas. These were more numerous in the right than in the left.

The *bronchial lymph nodes* were normal.

The *liver* was normal.

The *spleen* was normal.

The *kidneys* were normal.

The cultures from the right tonsil showed staphylococci and anthrax; from the left tonsil, anthrax. There was no growth on the cultures from any of the other organs, nor from the blood and the gastro-intestinal tract.

Histological Examination. Both tonsils showed somewhat similar lesions, though the infection was very irregularly distributed. While the greater part of the tonsillar structure was normal, almost all of the crypts contained an unusual amount of cellular debris, polymorphonuclear cells predominating. There were, however, some lymphoid cells and a large number of epithelial cells. In

a few crypts, staphylococci were present in large numbers and a few anthrax bacilli could be seen. The large majority, however, of the crypts contained no visible organism, even where the surrounding walls and tonsil parenchyma were extensively invaded. On the surface of the tonsil the predominating organisms were cocci, generally staphylococci, a few small bacilli, and an occasional anthrax bacillus. The surface epithelium was generally intact, though in places it was covered by a layer of necrotic tissue containing large numbers of polymorphonuclear cells and necrotic superficial epithelial cells.

Around the infected crypts the greater portion of the epithelium was either entirely destroyed, so that only a few scattered necrotic cells were visible, or it was so infiltrated with polymorphonuclear cells and lymphocytes as to make its outline scarcely distinguishable. There was, however, normal epithelium around a part of the crypt. In some places large numbers of anthrax bacilli could be seen between unaltered epithelial cells, being more numerous in the deeper layers. Near these places, that is, where there were anthrax bacilli in healthy epithelium, the neighboring interfollicular tissue showed only a few of the anthrax bacilli. The bacilli seemed to be passing in the direction of the lymph current, and in places the lymphatic spaces and some of the smaller efferent lymph vessels were choked with a dense network.

Another important finding was that anthrax bacilli tended to accumulate around the periphery of the lymph follicles, forming in places a dense ring around the edges of the follicle, with only a few scattered bacilli in its centre or in the surrounding interfollicular tissue. In the neighborhood of those crypts, of which the epithelium had been destroyed, the interfollicular tissue and also the follicles, showed the presence of numerous polymorphonuclear cells, congested capillaries, fragmentation of both the lymphocytes, and other cells, and quite a large number of free erythrocytes. Where the necrotic action was more marked all cellular contour had disappeared and the space filled with a striated non-staining debris. Anthrax bacilli were present in this necrotic tissue, seldom, however, accumulating in any great numbers. In a few places associated with the anthrax large numbers of staphylococci were found. Some of the anthrax bacilli situated in the unstaining necrotic tissue showed plasmolysis, otherwise these bacilli stained regularly and evenly.

The histological examination of the lungs showed that in the atelectatic area the alveoli contained a considerable number of free red-blood cells. Otherwise the lung tissue was normal.

Comment. The most interesting finding in this experiment was that the anthrax bacilli passed through normal epithelium, showing a tendency to multiply in its deeper layers. In the neighborhood of this invasion there were comparatively few

bacilli in the interfollicular tissue, while around the neighboring lymph follicle and in some of the mouths of the lymphatics large dense masses of anthrax bacilli were seen. Also the disease was entirely localized in the tonsils, there being no lesion in any other organ, nor could cultures reveal the presence of anthrax bacilli. Their absence from the gastro-intestinal tract must mean that in pharyngeal inoculation if the anthrax bacilli do not soon find a point of invasion they are swept away and destroyed by some agency in the gastro-intestinal tract.

Hog No. 3. March 26. Animal weighed about fifty pounds, and had been previously infected with sporothrix, and was also suffering from a traumatic myelitis. A twenty-four hour culture of virulent anthrax was rubbed over the tonsils.

March 29. Animal was killed with chloroform. Postmortem examination showed no signs of anthrax either in the tonsils or in other portions of the body.

Comment. This hog was an adult animal, and it may be that it had developed immunity to anthrax infection some time during its life.

Hog No. 4. April 16. A twenty-four hour culture of anthrax bacilli was rubbed into the left tonsil.

April 19. Animal was killed with chloroform.

Postmortem. Tonsils. On the left tonsil there were three or four elevated areas with a central necrotic core surrounding which was a zone of hyperemia; right tonsil, only one small area as described above. The mouth, pharynx, larynx, trachea, and esophagus showed perfectly normal mucosa. There was no enlargement of the lymph nodes of the neck, and the lungs, liver, and spleen were normal. A bouillon culture was made from the heart blood and agar cultures from the left submaxillary, left subparotid, and the right subparotid lymph nodes, also from the lungs, spleen, and liver.

April 21. All the cultures remained sterile.

Histological examination of the tonsils. Except for the rather small circumscribed carbuncles the tonsillar tissue was normal. The carbuncles penetrated deeply into the parenchyma and consisted of a necrotic core surrounded by a thick zone of inflammatory reaction. The area of disease corresponded in size and extent to a large crypt, of course, involving the neighboring parenchyma. Portions of the crypt wall were still found intact with normal epithelium, especially at its deep extremity. The surface epithelium covering the diseased area was necrotic, and the superficial layers were interspersed with numerous staphylococci. The anthrax bacilli was distributed throughout the diseased area, but were more numerous in the living tissue outside of the necrotic core. They were not found in the normal tonsil structure. There was a secondary invasion with staphylococci, and in one place there was a beginning abscess near the capsule of the tonsil due to this

staphylococci invasion. The staphylococci could also be found penetrating into the lymph radicals and accumulating on the periphery of one or two lymph follicles. The staphylococci had gained entrance to the parenchyma of the tonsil through an epithelial gap in the walls of the crypts. Just how these gaps in the epithelium had been formed could not be determined, but a few staphylococci were found free in these gaps, and quite a number engulfed in polymorphonuclear phagocytes in the parenchyma of the tonsil near this opening. The most resistant tissue to the action of the anthrax toxins were the *germinating follicles*, and these structures could be seen almost normal where the surrounding parenchyma had been entirely destroyed. The bloodvessels also showed great resistance, and were more numerous and larger than in the normal tonsil structure. The anthrax bacilli accumulated in large numbers around some of them and occasionally were found actually penetrating their walls, entering the blood current.

Comment. It is probable that the original invasion in this case was due to anthrax, and that there was also a secondary invasion of staphylococci. The staphylococci were enabled to gain access to the parenchyma of the tonsil because of the action of the anthrax toxine. The disease had advanced beyond a stage in which the anthrax bacilli could be seen in the living cryptal epithelium, consequently the mode of invasion could not be determined by this experiment alone.

Hog No. 5. April 24, 1913. Adult animal, weighed about seventy pounds. Rubbed an attenuated (at 42.5° C. for twelve days) twenty-four-hour culture of anthrax (vaccine strain B) over left tonsil.

April 28, 1913. Animal was killed with chloroform. Heart puncture made and blood taken into a bouillon tube for culture. On the right one there was a small carbuncle and a small congested area, while the left tonsil was apparently normal. There was no lesion in any other part of the pharyngeal mucosa or in the esophagus, larynx, or trachea. Cultures were made from the right submaxillary and retropharyngeal lymph nodes.

April 30, 1913. All cultures were sterile.

Histological Examination of the Tonsils. The tonsil in the region of the carbuncle showed very interesting changes. The carbuncle consisted of a central necrotic core surrounded by a distinct inflammatory zone. In the necrotic tissue large numbers of staphylococci were found and in some places they were seen penetrating into the living tissue of the inflammatory zone. Only a few anthrax bacilli could be found in the central part of the necrotic area, though they were fairly numerous around its edges. On the other hand, in the zone of inflammation, large numbers of anthrax bacilli were found. At places they accumulated, forming dense net-works, and also showed a tendency to gather around the periphery of the germinating follicles.

The diseased area was more or less associated in its topography with the position of a crypt, although it had, of course, advanced beyond the cryptal lumen and involved the surrounding tonsillar parenchyma. In some places the relation of the secondary infection of the staphylococci to the invading anthrax bacilli could be traced. The anthrax bacilli formed a distinct line of invasion in the living tissue and behind them the staphylococci were found in the non-staining material. The advanced necrosis in this position was evidently due to the secondary staphylococcic infection.

In another crypt, some distance from the carbuncle, a pure infection of anthrax bacilli was found. Surrounding this crypt the epithelium retained almost its normal structure, and yet large numbers of anthrax bacilli were seen between the cells penetrating into the surrounding interfollicular tissue. The bacilli, while fairly frequent between the superficial cells, accumulated in enormous numbers in the deeper layers of the epithelium and in the subepithelial tissue. The crypt lumen contained quite a large number of free anthrax bacilli. Portions of the surrounding interfollicular tissue showed congestion with beginning necrosis and there was considerable edema and extravasation of red-blood cells into the diseased area. The cells in this area stained poorly and there was fragmentation of their nuclei and other evidence of karyorrhexia. The anthrax bacilli congregated around some of the neighboring lymph follicles. While in some places they formed a net-work around the capillaries, the bacilli themselves were not seen in the blood current. The surface epithelium, except directly over the carbuncle, was intact and unaltered. In a few places along its surface a number of anthrax bacilli were caught and held in particles of mucus. The surface epithelium over the necrotic area had been destroyed and here large numbers of staphylococci were found, but no anthrax bacilli were seen in the epithelium itself.

Comment.—It is evident from an examination of this specimen that the anthrax bacilli gained access to the parenchyma of the tonsil directly through the unaltered epithelium of the crypts. Having penetrated the superficial layers of the epithelium, they seemed to proliferate in the deeper layers before passing on into the interfollicular tissue. The toxins, elaborated by the anthrax bacilli, however, evidently influenced the vitality of the epithelium so that it was readily attacked by a secondary infection, and it is probable that the greater amount of destruction was due to the secondary invasion of the staphylococci. There was no evidence that the anthrax bacilli passed through the uninjured surface epithelium. The slowness in the progress of the disease in this case was due to low pathogenicity of the infecting organism, an attenuated strain of anthrax bacilli having been used.

SUMMARY. From a study of the experiments as outlined above, we find several important facts which warrant us at this time in drawing certain conclusions:

1. The tonsils in the hog are more readily infected by the anthrax bacillus than any other portion of the buccal or pharyngeal mucosa. The clinical history of this disease in the hog shows that in a great majority of idiopathic cases, the pharynx is the site of the invasion, and in all of these cases of pharyngeal disease the tonsils are the portal of entrance. In none of my experiments was there any involvement of the pharyngeal or buccal mucosa other than the tonsils. While the culture of anthrax was generally brought into more intimate contact with one of the tonsils it was impossible to limit the bacilli to the tonsillar surface and they must have come in contact with a large part of the pharynx. At the inoculation an effort was made to rub the emulsion into one tonsil only, but in only one case (Hog No. 5) were the lesions limited to only one tonsil, and in this case the tonsil affected was not the one on which the culture had been rubbed.

2. Anthrax bacillus penetrates through the cryptal and not the surface epithelium.

3. Anthrax bacillus probably always gains access to the parenchyma of the tonsil by passing through the living, unaltered cryptal, epithelium, and having gained access through the superficial layers of this epithelium it tends to multiply in the deeper layers and then pass into the interfollicular tissue.

4. Anthrax bacillus penetrating through the living normal epithelium causes a devitalization of the tissue which paves the way for a secondary infection from the staphylococci or other pathogenic organisms.

5. The rapidity of the invasion is influenced both by the virulence of the organism used and by the susceptibility of the individual animal.

Following the invasion the subsequent course of the disease is similar to that found in other tissues. The toxin elaborated by the bacilli causes at first an accumulation of polymorphonuclear cells, later necrosis of the tissue cells with disintegration of the nuclei. The germinating follicles show more resistance to the disease than the interfollicular tissue. Associated with necrotic process is an increase in the number and engorgement of the capillaries, and sometimes there is marked extravasation of the red blood cells. The anthrax bacilli accumulate in the lymph spaces also around the bloodvessel walls. In some of the sections examined the bacilli were found penetrating the bloodvessel walls and a few were seen in the blood current. That these bacilli were not found in the heart blood was due to the fact that in anthrax the bacilli are held up in the capillaries until they have accumulated in numbers sufficient to overcome the vital resistance, when they are suddenly swept into the general blood stream.

ON SOME OF THE BROADER ISSUES OF THE PSYCHOANALYTIC MOVEMENT.¹

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IN bringing forward for discussion some of the more important practical considerations and scientific principles underlying the psychoanalytic movement, I have been moved by the belief that this movement marks one of the most important advances of modern medicine. It may need modification, supplementation and safeguarding, and its limitations will surely need recognition, but it cannot be ignored and it must be fostered, not by neurologists alone, but by physicians of all sorts, to whom patients with psycho-neurotic symptoms constantly apply for relief, and whose advice is sought with reference to the education of children who might readily become patients at a future day. It should be seen to be wrong, now that the causal mechanism of these disabling illnesses is so much better understood, that physicians should go on laying the chief emphasis, in explanation and treatment, on incidental disorders of some special organ, or on some abnormality of nutrition, or on the need of rest, or of suggestion or persuasion, provided the chance is at hand of getting nearer to causal influences which are far more fundamental. Various circumstances may compel the ignoring of these conditions, it is true, in given cases, but this should be done with the eyes open, and will become less often necessary when more men of high standing have been encouraged to fit themselves as experts for this work.

The psychoanalytic method of treatment is not simply one more means of palliation. It is based on a recognition of the fact that these patients are suffering from emotional conflicts the nature of which they cannot understand unaided, and is an attempt to make it possible for them to extricate themselves, through self-study and self-education, from the effects of these conflicts. It is not, furthermore, in its essence, a method which is dependent for its success on some unmeasured and subtle personal magnetism emanating from the physician. On the contrary, it is a system which anyone can learn who is willing to take the pains needed for this task. As a part of this system, the personal reactions of patient and physician on each other are made the subject of careful scrutiny, and subjected to constant control. The constant aim of every well-trained psychoanalyst is to encourage the patient to assume the responsibility for the success of the investigation, and to see that it shall result in a sense of complete independence on his part.

¹ Modified from a paper of the same title presented at the meeting of the Association of American Physicians, May, 1913.

Care should be taken to distinguish sharply between the merits of the psychoanalytic method as such, and the mode of its application in particular cases. Many physicians approve of the former, who think there is reason to criticize the latter, and such physicians owe it to their patients to test the correctness of this attitude by conscientiously studying the method, making it the basis of their practice, and applying to it such tests as they desire. No one can question the importance of a thorough anamnesis² as the foundation of a thorough treatment, and every student of human nature is aware that a man who is struggling with internal problems and false reasoning is in no shape to meet and solve external problems. But the aim and object of this method is just the securing of an anamnesis, of a thoroughness such as has never before been attained or even tried for, and the bringing home to each patient, in a form which admits of no misunderstanding (not only of reason but of feeling) the real nature of the conflicts through which he passed in childhood and is still passing. These internal conflicts form the natural problems in terms of which every growing child ought to build his rational and moral character, and a psychoanalytic treatment is simply one phase of a concentrated rational and moral education.

The results of the conflicts of our childhood do not die and disappear. On the contrary, they live forever, in an active form, and continue to produce effects, as integral forces, interwoven with the living fabric of our temperaments and characters, as determinants of our thoughts and conduct. It is, therefore, difficult to see why any student of education should fail to welcome this new means of rendering these conflicts clear and bringing them face to face with the intelligence and the moral sense.

It is often asked, "Of what benefit is it to make the patient intellectually aware of his long since repressed and forgotten emotions and temptations, and the frailties of his youth?" "Simply to see the terms and bearings of even a present temptation or perplexity is not equivalent to overcoming the one or solving the other; and as for bygone temptations and perplexities, once inadequately met, to be forced to rediscover them is to be made painfully aware of weaknesses which would better be forgotten and ignored. Repression is useful as well as harmful; it is a means of progress which was instinctively arrived at and found practically useful." Such is the general character of the argument.

But, in fact, although the intellectual presentation to one's self of the bearings and nature of a present perplexity or temptation is not equivalent to a moral or a rational victory, yet to arrive at such a presentation is the first step toward the victory, if the

² I use the word anamnesis only in the most general possible sense, and am well aware that it does not appropriately describe the outcome of a psychoanalytic investigation.

person tempted or in doubt really intends to make it such. And what is true in this respect of present conflicts is true also of old conflicts. For the latter still exist, and form, in reality, the main basis of the former; and arguments to the contrary, of the kind just cited, are apt to be only one of the many instinctive resistances that are built up as defences to preserve a *status quo* of invalidism, which is maintained by virtually the same influences that originally gave rise to it, and that made of it a means of compromise. Furthermore, it should be remembered that the final purpose of a psychoanalytic treatment is to conduct the patient's memory and insight back to that distant period of childhood when it was a question, not of being false to an obvious moral obligation but rather of slipping, half unwittingly, under the dominion of a strong craving, which then continued to make its power felt, by virtue of assuming ever new disguises. The patient—every person—must assume, later, it is true, the moral responsibility for the deeds and thoughts of this period of childhood, but if he is fortunate he may do so under the guidance of knowledge and of reason, and in doing this he may often work off his cravings, by stripping off their disguises, one by one, until it becomes clear just what it is that is leading him astray.

As for the assumed usefulness of "repression," it should be remembered that this is a word, like many more, of double meaning. It is a good thing to repress, on rational or moral grounds, and in the interests of sublimation, the desire to yield to a temptation which one clearly sees; it is a poor thing to close one's eyes to a temptation to which one really yields. One cannot, at one and the same time, cultivate real progress and likewise indulge in immature modes of thought and conduct which are hostile to progress in the best sense. The attempt to do this, even though unconsciously made, results in one or another form of compromise, which takes the shape of nervous symptoms or defects of character, both of which are often clearly traceable to the mechanism outlined.

It is well known that there has been a strong feeling of hostility to this movement on the part of some physicians, side by side with a strong confidence in its promise on the part of others, and that among its best adherents eminent psychologists and laymen of broad culture are to be found. An association largely made up of men whose work lies sufficiently outside of neurology and psychiatry to enable them to look at the matter with unprejudiced eyes should form a fair court of appeal, so far as this is possible where expert training is lacking. It would be impossible to discuss here all the grounds of the hostility to which I have referred. I shall have something to say later on the one point which really lies at the root of all the opposition, namely, the sex question; but I pause here to consider briefly one argument of another sort. It is not infrequently urged that patients are made worse by this

treatment, and individual cases are cited in verification of this statement. It is true that the very influences—partly innate, partly incidental, and largely of the sort here indicated—which induce the serious illnesses here in question, tend to weaken these patients' powers of coöperation and will to coöperate, so that the physician's mind must be made up for many relative disappointments; and it is easy to see how the hostile opinions to which I have alluded have arisen. If, however, adequate care is taken in the choice of patients, if the physician is well trained, and if the patient is in earnest, some good is almost certain to attend their combined efforts, even when complete recovery is impossible. Good results are not obtainable with equal ease in the case of all varieties of the illnesses for which this treatment has been used. It is generally conceded that the phobias and anxiety-neuroses are the most curable forms, while the compulsion-neuroses are less amenable, and the well-marked hypochondriacal cases still less so.³ But even the compulsion-neuroses yield more readily to this mode of treatment than to any other. That some patients do cling instinctively to their illnesses, and are ready enough to assume a hostile attitude toward the physician, or to minimize his part in bringing about improvements, is well known to everyone who has to deal, through any method, with psychoneurotic patients. An illness, unpleasant though it be, is sometimes instinctively felt to secure a better equilibrium and greater freedom from discomfort and from the necessity of struggle, than any substitute which appears to be in sight. This reasoning is, of course, unconscious on the patient's part, but it may affect his attitude, none the less, and he must learn to recognize this fact if he wishes to get well.

These statements may serve as an introduction to the next proposition, which has reference to the difficulties which the physician must encounter in fitting himself for adequately carrying out the psychoanalytic treatment. Except for these—very real—difficulties, the records of more frequent and thorough tests of the method and a greater number of critical comments based on personal experience, would doubtless have appeared.

While the first point that needs ever renewed emphasis is that through this treatment, as through no other to anything like the same extent, patients suffering from obsessions, morbid fears, and kindred symptoms can usually be enabled to see, and often to overcome their troubles, the next point is, then, that this task, though full of interest for both patient and physician, is not a light one. Any intelligent, careful person may utilize to some extent the principles worked out by the leaders of this movement, and may, through prudence and caution, avoid exciting in the patient, in

³ See a review of extensive experience by Dr. William Stekel, *Zentralblatt f. Psychoanalyse und Psychotherapie*, 111 Jahrgang, Heft 6-7, 1913.

any serious degree, the sense of dependence on the physician ("Uebertragung") which has so often proved a formidable objection to every kind of mental therapy; yet it is a very different affair to carry through really difficult cases to a successful issue.

Fortunately, the student of the future will have the great help of a comprehensive literature, and of the papers of practical advice which Freud and others have published during the past few years, and will, it is to be hoped, continue to publish. A careful reading of these admirable commentaries would make it clear to anyone that it is not alone a theoretical knowledge on the physician's part of the psychology of the "unconscious," and not alone technical skill, that is necessary for success, but that there is need also of self-restraint, patience, sincerity, and inflexible confidence in the ability of the patient to reveal himself, to his own advantage, if his will to do so goes deep enough, and the thorough-going adoption of the principle that no considerations of temporary satisfaction, on the part of patient or physician, should be allowed to override the main issues of the treatment, but that, on the contrary, both patient and physician should recognize from the outset that the task before them may call for material sacrifices on both sides.

It has, indeed, come to be recognized more and more by the leaders of this remarkable movement that one prominent cause of disappointment is the existence of defects or peculiarities of character and temperament on the physician's part, which blur the mental image that he seeks to form of the real patient, and unfit him for developing the patient's own powers as he might otherwise have been able to do. Few persons are so well endowed by nature as to be free from the liability to get these distorted images, and it is now looked upon as very important, indeed almost essential, that the psychoanalyst should himself have been through the same sort of self-examination, under the supervision of some expert, that he proposes to make use of for his patients. With such thoroughness in preparation presupposed, this field of work is certain to become more and more attractive to men of the best stamp.

The psychoanalytic movement, at its best, so far from tending to encourage lower ethical standards on the part of the physician, the patient, or the community, is certain to exert the opposite tendency. For every conflict implies an antagonistic action of two interests, one of which is certain to be more in the line of the best progress than the other. It is true that the progress which a patient makes in getting well is not necessarily of a very high sort, since the forces represented in some of our human conflicts may be between tendencies both of which might be characterized as relatively selfish. But, on the other hand, issues necessarily present themselves in the course of every psychoanalytic treatment,

which have to be met through the exercise of qualities of a better kind than those that had previously been most prominently in play, and frequently the moral influence of the treatment goes very much beyond this minimum. Psychoanalysis was primarily introduced, it is true, solely as a means of ascertaining the contents and influence of those tendencies in our lives of which it can be said, not only that they lie outside of consciousness, but that they are under the ban of "repression," and yet remain as objects of unconscious desire or craving. To render a person clearly aware of such tendencies as these is the first step toward making it possible for him to modify them and to utilize his knowledge for the evolution of his character. The task of the psychoanalyst has usually been considered to cease with the accomplishment of this first step. If he goes farther and helps the patient to study not alone the repressions of the sort thus far considered—that is the repressions of sensuous cravings—but also the dimly felt and crudely symbolized longings, intuitions, and aspirations, such as every person experiences but often regards with suspicion, incredulity, and even dread, and, in a sense, may be said to repress, yet which, if scrutinized and encouraged, may form the basis of fine character; if the psychoanalyst helps to the evolution of these *quasi* repressed tendencies, he becomes an educator in a far wider sense⁴ and thus enters on a line of work which entails new responsibilities and new necessities of preparation. Psychoanalysis is based on no system of ethics, and is committed to no special philosophy of life, though it does inculcate in an intensive form the sincerity and honesty which lay a good foundation, in one respect, for further development on these lines. In itself it represents a phase of education which corresponds mainly to the analytic element in the first two portions of Dante's pilgrimage into the life of the soul. The reasons for not going farther, and working definitely for sublimation in the widest sense have been reasons of a practical and cogent sort. In the first place, few psychoanalysts—few physicians, indeed, of any stamp—have had the training needful for this purpose. They have felt, with some reason, that to give moral education is not the function of the physician. In the next place the distinctive task of the psychoanalyst is so difficult, and calls for an expert training and a scientific attitude of such special sorts, that no one could do his profession or his patients justice, it has been felt, without devoting himself exclusively to the problems coming before him as scientific expert. If he attempted more, even if qualified to do so, he might perhaps accomplish less.

⁴ Froebel's remarkable scheme of education, thus far utilized almost exclusively for the kindergarten, contains a provision for rational retrospection and introspection which involves the principle of psychoanalysis. Consult Miss Susan E. Blow's recent and interesting Report on the Kindergarten.

I regard these views as sound, but do not think they altogether meet the point at issue.

Psychoanalysis is, after all, a phase of education, and has been characterized as such by Freud himself. Education is of different sorts, but the goal of every kind of education is in a measure determined by the nature, origin, and destiny of the human mind, and the psychoanalyst of the future is likely to profit greatly through the recognition of this fact. This great movement cannot steer its difficult course or accomplish its whole mission under the exclusive guidance either of biogenetic methods or of those principles which the students of the processes of inorganic nature have worked out for their particular needs, and have so often and so erroneously assumed to be final statements of the truth. For these principles do not by any means fully explain the working of the mind, nor account for the *origin* of the instincts or tropisms which are supposed to foreshadow mental action; and, moreover, the too exclusive study of these principles is liable to turn aside the attention from others, of still greater value, which refer mind, instincts, and chemical processes alike, to the influence of a self-renewing, self-active energy, seeking fuller and fuller opportunities for self-expression.

I cannot pursue this argument further here, but assert as my opinion that the study of the vitally important relationship between the life of the individual and the total life of the universe, and the adequate study of the laws of mental action, will afford a basis, of a much needed sort, for the understanding of the true place of the psychoanalytic phase of education on a more comprehensive educational scheme. It may well be that among the qualifications considered essential for the psychoanalyst of the future, certain sorts of training which are now thought little of will be included. Certainly the only logical stopping place of a complete psychoanalytic treatment is a complete "sublimation."

The psychoanalyst must indeed be a scientific expert, eager to see his special art advanced, and this need must be considered paramount to every other. But in every department of learning there are men whose powers best fit them for the exclusive study of some special problem, and others who do better service, even in detail, if they see each special problem on the background of a comprehensive scheme.

It will have been made evident by the trend of the foregoing statements, even if not already known, that the main emphasis of psychoanalytic investigation and treatment has gradually been shifting more and more toward the apparently forgotten years of infancy and early childhood—that mysterious and eventful period which is more significant than any other for the formation of character and temperament, and for the establishment of tendencies of mental reaction from which it is exceedingly difficult, afterward,

to depart.⁵ No more important task lies before the psychiatrist, the psychologist, or the educator, than the study of these tendencies—both those which help toward the realization of the best possibilities of development, and those which act to turn aside or turn backward the forces through which these results might have been attained.

It is needless to say that the facts and inferences thus brought together are not wholly new; they are all the more significant for not being so. Neither can the results of psychoanalytic studies, which are of necessity made largely on persons who were preëminently handicapped at the outset, in the race toward the higher goals of life, be substituted at every point for observations made on those who have, from the beginning, been inspired by a clearer vision of these goals; nor can the experiences of the child be said to foreshadow in every respect the experiences of the adult. The adult can form and follow ideals and motives which he could not have appreciated as a child, but he must reckon, consciously and voluntarily or instinctively, with his childhood tendencies in so doing, at the cost of carrying a constant handicap if he neglects this obligation.

We are so used to seeing the greater number of our children develop rapidly on fairly satisfactory lines, so habituated to seek in them for signs of mental characteristics familiar to us and into possession of which they are to come, later, and so little used to referring the evidences of their later troubles to tendencies first emphasized in infancy and early childhood, or to form any adequate conception of what passes in their unconscious minds, that only the close observer learns to recognize the extent and number of the chances of going wrong, to which all children are exposed, and in meeting which they react in such a fashion as to establish models for the reactions of their later years.

It would seem that the infant's mind is a more complex instrument than has usually been supposed. There is reason to believe⁶ that the newborn child brings into the world a certain familiarity with various feelings and sensations with which there must go a dim consciousness of himself as experiencing them. Not only this, but there is a possibility, which we probably underrate, that not only isolated perceptions, but complex, though vague, emotional states, capable of being dimly recorded in memory, may be present before and during birth.⁷ Be this as it may,

⁵ The most important data for a psychology of childhood based on psychoanalytic research are furnished by Dr. von Hug-Hellmuth's recent monograph, *Aus dem Seelenleben des Kindes*. See also review by the same author, under the title *Kinderseele*, in the *Imago* for February, 1913, vol. ii, 1.

⁶ See F. Peterson, *The Beginning of Life in the New Born*, New York; also, Ferenczi, *Internat. Zeitsch. f. Aerztliche Psychoanalyse*, vol. i, p. 2.

⁷ Dreams and reminiscences hinting at vague but impressive birth-memories have now been reported in considerable number.

it is certain that the infant begins quickly to classify the masses of new sensations that are poured in upon him, in accordance with principles of emphasis which are quite different from those that are characteristic of the adult, or even of the older child, who has learned to shrink with a disgust that often overshoots its proper mark, from many of the sources of personal gratification congenial to the period from which he has escaped. To the infant, it would seem that every experience, partly in virtue of its novelty, is capable of yielding a special charm; and if fear soon enters to complicate the situation, even this has a certain fascination of its own to offer. From the standpoint of the emotions based on the cutaneous and muscular sensibility, it is certain that the act of nursing, the rubbings, caressings, dandlings, bathings, the warm contacts applied to large surfaces of the body, the processes of digestion, the acts of defecation and urination (that is, especially the orifice stimulations), the chance excitation of the genital organs, the movements of the limbs, often give rise—over and above the sensations and other reactions which are usually accredited to these sources, as accompaniments of normal development—to pleasurable feelings such as every adult knows and has perhaps learned to deprecate, and to classify as “sensuous,” though he may have long since dissociated them from these special causes and is unaware of the purpose which they once served. To the child these sensuous feelings are, at first, natural, acceptable, and free from connotations of deprecation. To the adult, the very thought of what might be called the nursing and diaper period of infancy is displeasing, at least in many of its details, which savor of dirt, humiliation, and dependence; and he fails to do justice to the physiological and psychological value of all these attributes of this portion of his childhood as preparing him for the important functions of his later years.

In fact, however, it is not harmful or reprehensible, but necessary and desirable, that the infant and the child should devote much attention to their own personalities and powers—that is, that they should be duly egoistic—and necessary and desirable, also, that they should find their attention engrossed, up to a certain point, by that special element in the various experiences just referred to [and their number could be indefinitely extended] to which, later, the name of sensuousness is given, with its adult connotations of reprehension. The objection is not to these emotional states as such, but only to their being allowed to play too large and too engrossing a part, that is, to their being too long cultivated, in and for themselves alone, that is, simply as a means for the intensifying of personal excitement and self-indulgence, instead of as a stepping-stone to something better. The intense egoism of childhood, which is led up to by the discovery, on the part of the infant, of his power of obtaining these sensuous forms of gratification, is of great value as a means to a normal self-asser-

tiveness and individualism.⁸ But egoism has its strongly sensuous aspects, and may lead to a too literal self-love (narcissism), properly classifiable as a species of sex-craving, or, like all forms of sensuous pleasure, may induce an excessive revolt (over-sensitiveness, morbid self-consciousness or self-reprehension, etc.), which is equally objectionable and on exactly similar grounds. The child who takes the middle course of safety, and who at the same time, preserves and assimilates something of good from the contemplation of the dangers by which he is surrounded, is a child of superior order, though, fortunately, the outcome which we designate as normal admits of many and considerable variations, within a wide margin. The dangers and the liability to go wrong would doubtless be more apparent, were it not that the tendencies toward the better forms of evolution have developed an instinctive power of surmounting these dangers with relative success.

In other words, the child must be sensuous (in the best sense) up to a certain point, but not beyond. Furthermore, he must not revolt too strongly against an assumed excess of sensuousness in any particular respect; for this revolt will then become a source of danger—practically a craving—in its turn. Through his first dealings with this difficult problem of sense-pleasure, to which every month and every year adds some new element of complexity, the child forms or emphasizes a series of tendencies which are likely to characterize his acts and thoughts throughout his life. He cannot be expected to exert effectively a power of control and a sense of obligation which as yet are hardly born, and the result is that, to a greater or less extent, he is bound to develop on a double plan and to prepare himself to lead a more or less double life—the life of conscious and obvious acquiescence and social relationship and the life of private and concealed fancy and emotion. This latter life he must, moreover, lead, for the most part, alone, for there is no one who can thoroughly understand the symbolic language in which he is defining to himself his new world.

Even under the best conditions the particular kinds of pleasur-

⁸ Closer students of this subject are aware that there is a group of psycho-analysts, whose main representative is Dr. Alfred Adler, of Vienna, who think that the main, fundamental craving against which the young child is compelled instinctively to strive is this very need of self-assertion, the need of feeling that he is taking his place as an individual "against all comers," and that he must at least fortify himself with a feeling that he is doing so, even at the cost of self-deceit (*Siekerungstendenz*). Dr. Adler takes the view that the sensuousness, or sexuality, of the child is, for the most part, only the form in which this self-assertion strives to find expression. The facts and arguments adduced by him and others are exceedingly interesting, but cannot be done justice to in this place. In general terms my own opinion is that the excessive self-assertion and the sensuousness, self-indulgences, and egoisms are, all, imperfect attempts at self-expression which has a deeper root, and in view of the fact that even self-assertion, feelings of personal relationship, are present either toward oneself, or toward others who stand in intimate connection with oneself, the sex element cannot be excluded, and will continue to represent at bottom the principal repressed element in human life, in a relative sense, at least. To say this is not to deny, of course, that self-assertion, with the "*Siekerungstendenz*," may be the goal for which most persons mainly strive.

able sensation that first engrossed him are likely to establish goals toward which, in unguarded moments, (as in dreams and fantasies) and in times of stress, he will be likely to revert, just as we all gladly revert, in minor degrees and ways, to simpler conditions of living, for compensation or refreshment. The strength of the tendency to this reversion is measured by two factors, the intensity of the original engrossment and the degree to which it was instinctively put out of sight ("repressed"), in the first instance, so that its presence as a temptation could no longer be directly seen. For an instinctively repressed temptation is one that continues to exert its action, but in a concealed form and under new names and forms. It is this quality of engrossment, combined with this fact of its early repression, that gives the sensuous element in the life of childhood its great significance, over and above its importance as preparing for the functionally sexual life of adolescence. On these grounds the life of infancy and childhood is properly described as strongly (though, of course, only partially) "sexual:" (1) because of the sensuous elements in it which actually pave the way for a normal or an abnormal (inverted or perverted) sexual development; (2) because the child tends to take himself (self-love, narcissism) and those about him (mirror-love in a new form; premature and overstrung homosexual or heterosexual attachments) as objects of a too passionate engrossment.

Infants and children evidently differ enormously as regards their liability to be engrossed by these peculiar sense seductions, on the one hand, and in the degree to which, on the other hand, they feel, in its infantile form, the inspiration and the spirit which is to show itself later as a noble sense of disinterestedness and obligation, commensurate with the best possibilities of the future. But the existence, in a certain degree, of egoism and sensuousness (*sit venia verbo*) in the period of infancy is not to be taken as a sign of recreancy to natural trust and duty.

One great task lies before every child—to make himself a useful member of the community in the widest sense.⁹ But a vastly important portion of this obligation lies in learning to play his part, suitably, in the perpetuation of the race. The incitement to this task is provided for by nature with the most jealous care, as indicated by the vast multitude of seeds that must perish in order that one may germinate. Not during adolescence alone are the incitements to the accentuation of the sex-emotions infinitely numerous and infinitely subtle; not in adult life alone is the temptation a serious one to the cultivation of pleasures, which though capable of being eminently useful, are often not only negative, but harmful, in their relation to the best possibilities of development. The incitements and the temptations to abuse of such incitements present during

infancy and childhood, are equally numerous and all the more difficult of avoidance because unrecognized. The child who is "sensitive" or "precocious," or whose fancy is unregulated, is on the danger-line, and that child is fortunate whom, from the outset, a dim vision of his best possibilities, a dim sense of obligation to a cause greater than his own—represented by the sense of obligation to parents, nation, or to an assumed universal personality more vast and significant than these—so inspires and guides that he is able to make the sensuous pleasures of his infancy his servants and not his masters. That this result fails, with tragic frequency, to occur, is testified to by the frequency with which lives which seem to be surrounded by all the outward conditions for great happiness become the battle-ground of miseries, tempered only by longings for a better fate and also by the commonness of the occurrence of the serious neuroses and psychoneuroses, which represent the compromises of tempted childhood, half aware of its better possibilities. Fortunately, even a belated enlightenment and the chance to discuss one's inner conflicts with some one who has been trained to see them in the clearest light may still be helpful. For in proportions as knowledge, reason, and insight prevail, unreasoning and passionate emotion is apt to fade away. To give the best chance for the reinstatement of knowledge, reason, and insight is the function of the psychoanalytic treatment.

What is true of the sensuous element in the period of infancy is quite equally true of various more complex groups of emotions, which are closely related, in genesis, to those just mentioned, but are more characteristic, though only relatively so, of later periods of life. I have reference especially to the sense of power¹⁰ or superiority or self-assertion, with its accompanying opposite,¹¹ the sense of inferiority and submissiveness—both of which may contain a truly sensuous element—or to the excitement of causing or submitting to pain. The complex fascination from these sources lasts, as a rule, the lifetime of every individual, and plays an important part in the determination of his conduct.

I am, however, not undertaking to describe at length the life of childhood. To do this would take us far into the nursery and the kindergarten and the playground, and make necessary a deep study of the extraordinary character of the life of fancy of even the youngest child.¹² My only purpose here has been to bring into relief the character of the problem with which psychoanalysis, as a therapeutic agent, seeks to deal. With this aim in view, I have

¹⁰ Cf. the exceedingly interesting discussion by Ferenczi (*Internationale Zeitschrift f. Aerztliche Psychoanalyse*, vol. i, H. 2) of the sense of power developed in the mind of the newborn child by the conditions of his life and care.

¹¹ *Loc. cit.*

¹² Cf. the very important study by Bleuler (*Jahrb. f. Psychoanalyse, etc.*, vol. iv) entitled *Autistisches Denken*.

desired to intimate that, on the one hand, and as if in the far distance, there stands a goal of possibility of individual development, to which, fortunately, every child is strongly drawn by bonds which he could not himself define and does not even realize the existence of; while, on the other hand, he must work his way along, like Ulysses passing the Sirens, like Christian passing through the Valley of the Shadow of Death, in the presence of only dimly appreciated dangers, which we are now beginning, for the first time, clearly to understand. The ordinary forms of failure in this enterprise lead to the ordinary forms of nervous invalidism, or to one or another familiar defect of character; and in every such case, at every period of development, signs are to be detected through appropriate tests, unless the process has terminated in recovery, which indicate that the original temptations to make too much of particular sense-pleasures in and for themselves, have given place to new forms of temptation in which the same emotional tone is present.¹³ It is not necessary that these new and ever changing signs should point to gross sensualities of any sort. One and the same act on thought may serve to indicate, at the same moment, something of a man's spiritual nature and something of his sensual nature, and in every act or thought something of both of these elements may find opportunity for expression.¹⁴ The more serious forms of failure lead to inversions, to perversions, and to criminality.¹⁵ The extreme outcomes, of success on the one hand and failure on the other, in the development of the child, are determined, obviously, by strong influences which are not to be classified in any single category. These extreme outcomes are, moreover, so different in aspect and apparently so opposed in nature that when either set of them predominates, the ordinary observer may fail to appreciate that in every case both are really active. Any child may *play* criminal almost to his heart's content; and perhaps every

¹³ I believe that it would be of more psychological value, instead of using the expression "emotional tone," to choose some term which should be equivalent to "generic or creative energy," using this term as it has been used technically to express an idea underlying a series of manifestations. The generic energy of a tree, for example, covers the whole series of forms comprising the cycle of growth of the tree. In other words, it would be profitable to bear in mind, as I have hinted in another part of this paper, that in dealing with these phenomena of immaturity, under the different forms in which they manifest themselves, we are dealing with forces and tendencies which might be compared analogically to other process groups with which observation has already made us familiar, as classifiable under one or another heading.

¹⁴ It is important for the rational interpretation of the symbolism of dreams and conduct, that this point should be clearly understood. It is often urged that those who use the psycho-analytic method are too prone to read sexual meanings into trivial and harmless thoughts. But, however, this may be in a given case, it is certain that the ingeniousness of psychoanalysts in this respect does not equal the ingeniousness of persons of emotional temperament (patients, poets, and artist) in finding means to express the sensuous elements of their nature which they have brought over from their childhoods. Any symbol can be made use of by the lover to intensify his passion and find new outlet for it. But that does not prevent the employment of the same symbol for some other end or ends. These facts and their bearing would be recognized were it not that the very hint at the possibility of sex-meanings gives rise, unjustly, to opposition and resentment.

¹⁵ It is, I trust, needless to say that I am now dealing with the psychogenetic factors alone, and that I realize fully the existence, likewise, of somatic factors.

child, as a necessity of biological and psychological development, shows tendencies which, if they persisted and grew stronger, would mark him as an invert or a pervert. But so powerfully does the current ordinarily set, in the one direction or the other, that we feel entirely safe, as a rule, as regards the future of the greater number of our children, and consider that those who go right and those who go wrong are separated by differences almost as great as those that distinguish from one another the different animal species. It is only when the chance is offered for getting at the real facts, and especially for clearly facing the repressed tendencies and experiences of the life of childhood, that these differences are seen to be of degree only, and that we learn to appreciate that all children grow up in a broad borderland between the evil (as we classify it later, not as it appears definitely to the child) and the good. Many an adult, every individual in some measure, is more or less under the spell of this or that tendency which harks back directly to one or another special craving or sense—fascination of childhood or infancy, which was then, though perhaps only for a brief period, felt in full intensity, but promptly repressed and relegated to the unconscious.¹⁶ But by this "repression" these special cravings or fascinations are placed in a position of advantage for continuing to exert their influence, always in covert ways and in constantly changing ways, without ever, perhaps, coming under the full light of conscious, rational inspection, though constantly giving rise to emotional distresses and nameless fears, and an ill defined sense of something wrong. Strangely enough, these distresses and apprehensions are bound to the fascinations which preceded them by bonds which show them to be of common nature, and are instinctively clung to as representing, in terms of the patient's unconscious logic, the once legitimate though soon repressed pleasures of the age of childhood.

Just what the original fascinations of childhood are I have been able here only distantly to hint. Every observer will admit, however, that such fascinations exist; that they are very numerous; that every child's vivid fancy¹⁷ is fertile in inventing them; that they might be classed primarily and broadly as egoistic; that they are of a kind that it is easier to acquire a taste for than for those which are to be useful for the higher spiritual development of the individual, and that for this reason they are constantly reverted to in times of even moderate stress. If it is just to classify as "sensuous" these vague, voluminous, personal, egoistic, mirror-love sorts of pleasures, which are ill-defined, but intense, and full of

¹⁶ The tendency of persons of extreme refinement to show, in the deliria of mania or the rambles of dementia præcox, a familiarity with subjects and language assumed to have been wholly foreign to their thoughts, has always been a matter of painful comment and surprise. In fact, such patients thus disclose a very important chapter in their development.

¹⁷ Reproduced in the delirious but really consistent utterances of many insane patients, especially in dementia præcox. See Bleuler, *loc. cit.*

captivating thrills, it is just also to recognize that the quality which is most characteristic of them is most strongly present in those special sensations and emotions which are particularly and specifically related to the sexual functions, and which, as such, enjoy a special primacy as regards psychological and physiological significance. But these sensations, acts, and emotions—both those which are frankly sexual and those which contain the sensuous characteristics of the sexual feelings as a constituent element or are readily drawn into the great vortex of which the sexual feelings and emotions form the centre—are largely repressed, in deference, partly to the child's fastidiousness, partly to his conscience (both of which have a social root), and partly to the spoken or unspoken wishes of a social environment in which the interests of individual members are subordinated to the assumed interests of the social group, regarded as a whole.

The situation of the young child is a difficult one; and so, too, is that of the adult who is the child grown large and who is tempted to play the child's game with the grown-up weapons of the man. A man is filled with dread¹⁸ lest he may injure some member of his family whom in fact he loves, and perhaps isolates himself in consequence. But psychoanalytic study shows that in reality he is reverting to his childhood and is playing the old childhood game of love, hate, desire, fear, anger, sorrow, jealousy, and remorse, —each emotion acting at once as the parent and the child of its opposite and each capable of passing into the other or suggesting its opposite or of intensifying itself through inducing a thrilling sense of contrast with an undefined opposite. In childhood, the first and strongest of these emotions is desire, especially, desire of the sort that is particularly characteristic of the sex-feelings and emotions, which, instead of being absent, in infancy and childhood, are both present and engrossing. And so it is that when the conscience and the will relax, and the longings hark back to less strenuous and more immature and infantile interests, the emotions which come to the front are necessarily those which it is proper to denominate as sexual, since it is round the—biologically and socially—enormously significant sex-instinct that these interests and emotions cluster, and from it that they gain their color, and their emotional tone. Having learned all these and many other kindred facts, we can no longer wonder at Freud's dictum, that no psychoneurotic (emotional) illness can possibly occur without a concomitant, and partly causal, ruffling of the vast waters of the sex-life.

In searching for a simile through which to illustrate to myself the strength of the bond by which the development of the child is restrained in this or that respect, through influences of varying sorts, I have been able to find none so useful as that of the massive

¹⁸ I have, of course, specific histories in mind.

"fixation"¹⁹ or "arrest" that brings about the formation of the various animal species as an alternative to the continuance of the line of progress toward higher types. It is needless to say that I attach little or no biological importance to the comparison.

When the case presents itself of helping to recovery a patient in whom these tendencies to arrest have become established, it is of great service to him, not alone to be shown clearly the path toward a better evolution of his personality and powers, but to be helped to put himself back again, in memory and imagination, at the point where the partial arrest occurred, in order that he may see clearly what a different choice, at that point, would have accomplished for him, and that he may even now make it, as if for the first time, and thus rid himself of a craving which had gained a strong and yet fictitious power over him. But these processes must be conceived in psychological terms. Each individual must learn to see himself and the physician must learn to see him, as a collection of interwoven forces, all still living and still active, even though many of them came into existence in the early days of childhood. And the physician who does not possess by nature, or cannot acquire, the power of thus reading the lives of his patients in the terms of these living forces, is not at all likely to find satisfaction or success in psychoanalytic practice.

No one can make the best use of his powers, either for his personal happiness and guidance or in the interests of the community, who is the victim of his own immature passions, prejudices and superstitions, and who continues through adult life to use his imagination for inventing an unreal world of which he is the centre and the hero. Such a person should be aided to destroy this great structure of a misguided fancy and self-love, by learning to see that from its foundations upward, it misrepresents his best desires. A sound moral education should not tend to stifle emotion but to see that it is directed toward the best goal. The child's danger is that he will misuse the great forces which are placed within his grasp, for his own personal gratification, and one form, not yet clearly alluded to, in which he does this, is in playing with his own heated emotions, under the guise of imaginary danger. Every child, even if at bottom cowardly, loves to play at the game of Phaeton, assuming, in ignorance and folly, to drive the wagon of the sun. He loves to dally with himself and to create mock dangers and mock fears, in ways that by no means necessarily fit him to meet the real dangers of the coming world. He loves to excite himself with fire and the dark, and with fancies of death and life, not realizing with what deep, emotional interests he is dealing. But this emotional fire must not be too hot. When that point is reached the fear becomes a real sense of terror, and then the child, ignorant that the cause of his putting himself into the dangerous

situation was his (covert) love of what the adult calls sensuous pleasures, finds himself forced to explain or "rationalize"²⁰ his fears. The fascinating flame becomes a "cross" to him, and he begins to refer his distress to one or another common cause of dangers. One may represent this situation by drawing a flame and a cross, side by side, on a sheet of paper, with a line between them to indicate, so to speak, that though in reality mutually dependent, each is unconscious of the other. If, now, the patient would recover, and cannot do so through the interest of work, or by the attempt to get into a spiritual atmosphere above the fear, he must learn to turn his attention wholly aside from his symptoms (his "cross"), the contemplation of which he is certain to have followed too long, and to too little purpose, and must study the flame, that is, he must study the history of his emotional life. An intimate acquaintance with this history, by teaching him the real nature and origin of his fears, and showing them to be fears of himself, puts him in a far better position for attaining that development of character through which he may get well. Then the cross, in the old sense, disappears, but may still be voluntarily accepted as symbolizing the willingness to endure sufferings, not indeed of the sort formerly endured, but of a sort which will make the patient better able to take his place as a useful member of the community. The person who has attained this development has learned, in Emerson's words, that "when half-gods go the gods arrive," the half-gods being his own immature desires. What every person wants is happiness and content. But these are to be gained, as a rule, not by the cultivation of pleasures of the kind that exist in and for themselves, but rather through disregarding them in the interests of a broader life.

It is one of the remarkable signs of the far-reaching significance of the freedom with which we are endowed that we can use it to destroy our freedom; and a striking illustration of this is seen in the subtle, instinctive keenness with which the young child, when not sufficiently impelled by his own natural resources and not sufficiently aided by education, instead of taking each stage in his development as a stepping stone to the next, grows old indeed in years, but clings nevertheless, in secret, and without fully realizing the fact, to childish forms of thought and emotion which should have been outgrown and of which, even as a child, he was perhaps secretly ashamed. Clear sighted educators have long known the importance of this principle in the case of children somewhat older than those that I have now in mind. But it has remained for this group of investigators and those who have gradually affiliated themselves with them, to discover, point by point, the influences, which lead to the formation, in the hidden depths of the child's mind, of emotional modes of thought and feeling (*Autistisches Denken*, Bleuler) destined thereafter to play a large part in the

determinations of his conduct. The emotions and excitements of this autistic life exist largely, not as transitions to something better and more permanent, but in and for themselves alone. Even though not consciously perceived they act to draw the desires away from the disinterested forms of love which constitute the natural goal of progress, and tend instead to the cultivation of egoistic forms of love, which may indeed have an object, but use that object as a mirror by means of which self-love may be intensified. The fantasy-life of young children may serve as the basis of wholesome forms of religion and art, but sometimes, instead of this, it serves as the basis of morbid tendencies and morbid fears.

The evidence is very strong for the view that the appearance of the human mind among the evolutionary forces²¹ introduces a new factor of enormous import. Even the infant and young child, by reason of the endowment of their mental structure, have powers and obligations which they, however, cannot easily or fully recognize. With their consciousness of themselves they acquire also the germs of consciousness of the scheme of the universe. They acquire the sense of power, responsibility, and personality, and also of weakness and dependence upon others and the subtle pleasure that goes with dependence. With their unbridled fancy they people the world and they utilize not only sticks and stones but everything, even their own sensations, as terms in which to express their passions and desires and longings. Then come reactions, loathings, self-depreciations, and forgetting in the form of repression, which means really not forgetting but setting aside for further use. The child who is living externally a life of eminent self-satisfaction and propriety may be indulging himself, without knowing it, in the aroma of pleasures and excitements which he had banished to the "unconscious," but to which he still keeps many secret avenues open.

How can a treatment through which the patient is enabled to see what is going on and to unmask the "confidence game" played by his lower nature on his higher nature, fail to commend itself as worthy of support? The method which attempts this should, moreover, be judged with reference to its possibilities, and not to its present achievements only. Its aim, in general terms, is to help toward the solution of the external problems of human beings, by helping them, in specific ways, to solve their internal problems.

And this is a reasonable task. For the drama of the external world is played over, beforehand, in the minds and hearts of the personalities by which it is peopled. Let those who believe in the value of the method, but object to the way they think it used, test it out themselves. They owe it to their patients to attempt this task.

²¹ Attention has been called by Bergson and many others, to the significance of "life" (*poussée vitale*, etc.) as a factor in evolution. The doctrine of which I now speak includes this, but goes beyond it.

AN IMPROVEMENT OF THE BENEDICT METHOD FOR THE DETERMINATION OF SUGAR IN THE URINE.

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Benedict's¹ sugar titration method is conducted in the following manner:

"The urine, 10 c.c. of which should be diluted with water to 100 c.c. (unless the sugar content is believed to be low), is poured into a 50 c.c. burette up to the zero mark; 25 c.c. of the reagent² are measured with a pipette into a porcelain evaporation dish (25 to 30 cm. in diameter), 10 to 20 grams of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice stone or talcum, and the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The diluted urine is now run in from the burette, rather rapidly, until a chalk-white precipitate forms and the blue color of the mixture begins to lessen perceptibly, after which the solution from the burette must be run in, a few drops at a time, until the disappearance of the last trace of blue color, which marks the end-point. The solution must be kept vigorously boiling throughout the entire titration. If the mixture becomes too concentrated during the process, water may be added from time to time to replace the volume lost by evaporation. The calculation of the percentage of sugar in the original sample of urine is very simple. The 25 c.c. of copper solution are reduced by exactly 50 mg. of glucose. Therefore the volume run out of the burette to effect the reduction contained 50 mg. of the sugar. When the urine is diluted 1 to 10, as in the usual titration of diabetic urines,

¹ Benedict: Jour Amer. Med. Assoc., October 7, 1911, p. 1193.

² The solution has the following composition:

	gm. or c.c.
Copper sulphate (pure crystallized)	18
Sodium carbonate (crystallized)	200
(Or one-half the weight of the anhydrous salt may be used)	
Sodium or potassium citrate	200
Potassium sulphocyanate	125
Five per cent. potassium ferrocyanide solution	5
Distilled water to make a total volume of	1000

With the aid of heat dissolve the carbonate, citrate, and sulphocyanate in enough water to make about 800 c.c. of the mixture, and filter, if necessary. Dissolve the copper sulphate separately in about 100 c.c. of water and pour the solution slowly into the other liquid, with constant stirring. Add the ferrocyanide solution, cool, and dilute exactly to one liter. Of the various constituents, the copper salt only need be weighed with exactness. Twenty-five cubic centimeters of the reagent are reduced by 50 mg. of glucose.

the formula for calculating the percentage of sugar is the following:

$$\frac{0.050}{X} \times 1000 = \text{per cent. in original sample, wherein } X \text{ is the}$$

number of cubic centimeters of the diluted urine required to reduce 25 c.c. of the copper solution."

In this modification of the original Fehling process, the copper, instead of being reduced to the red suboxide, which of its own color obscures the end-point of the reaction, is precipitated as cuprous sulphocyanate, a snow-white compound, "which is rather an aid than a hindrance to accurate observation of the disappearance of the last trace of blue color."

However, in applying Benedict's method to urine of low sugar content, below 0.5 or 0.4 per cent., as is frequently the case in glycosuria, one is impressed by the fact that there is no blue color at the end-point that could disappear, the contents of the porcelain dish then having a dirty, brownish-green hue, that gradually merges into brown. This renders the correct estimation of the end-point difficult, if not impossible.

This condition naturally suggested clarification of the urine, previous to titration, by the addition of lead acetate. This procedure, while helpful, requires additional manipulations and calculations. The possibility of a chemical change of the copper solution is another objection to the use of lead acetate.

None of these objections apply to the simple modification the writer has been investigating. It consists in the addition, just before heating, of approximately 10 grams (two heaping teaspoonfuls) of powdered calcium carbonate to the contents of the porcelain dish (25 c.c. of Benedict's solution, 10 to 20 grams of crystallized sodium carbonate or one-half the weight of the anhydrous salt, and a small quantity of powdered pumice stone). Thereupon the titration is conducted in the usual manner.

The snow-white calcium carbonate, insoluble and suspended in the alkaline solution, appears to act in a manner similar to that of sulphocyanate of copper, by effectively obliterating all color except the blue of the unreduced copper compound.

The end-point obtained is sharp, the blue color being visible up to the addition of the last two drops of urine that are necessary for complete reduction, a pure white residue remaining. It is necessary, however, to add a sufficient amount of calcium carbonate, about 10 grams, otherwise the residue will appear gray and the end-points less distinct.

In order to prevent sudden violent ebullition of the hot concentrated solution, it is advisable to dilute the latter with a few centimeters of distilled water.

The writer's experiments show that the addition of calcium carbonate, as recommended above, does not cause any unfavorable effect on the accuracy of the titration.

THE APPLICATION OF THE CALCULUS TO THE MEDICAL SCIENCES.

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IN the following I am giving a few ideas on the above subject in connection with a Calculus recently published, entitled *Einführung in die Höhere Mathematik für Naturforscher und Aerzte*, by Dr. J. Salt peter.¹ It is a book of unusual merit. The representation is rigorous and lucid. The book contains many examples illustrating the application of Calculus in developing mechanical and chemical laws and processes. Although the author has intended the book for the use of students in the natural sciences and medicine, it is equally well adapted for engineering students.

The applications of the Calculus to the different branches of the medical and allied sciences is of comparatively recent origin. The originators are still with us. The science of mathematics is new. It is only about 200 years since the Calculus was invented (Leibnitz, 1646–1716 and Newton, 1642–1727). The first account of it was published by Newton in 1693. But the real advance of the mathematical sciences has taken place during this and the last generation. The application of Calculus to any of the sciences including the technical sciences, dates back only to the middle of the last century. Most of the schools of engineering in this country and abroad have been founded within the last fifty years or so. The scientific development of all the natural sciences does not date very far back, and the makers of the sciences have died within our generation or are still living.

I recall the address delivered by the founder of scientific pathology, Rudolph Virchow, before the students of the University of Berlin on the occasion of his seventieth birthday (1891), at which he entertained his hearers with an account of the most incredible theories and absurd views that prevailed in natural science when he first began the study of the subject.

In this connection it is interesting to read the presidential address of Dr. S. Weir Mitchell to the Congress of American Physicians and Surgeons held in 1891,² from which I quote the following (p. 163):

“When I was yet a lad there were then alive men who could recall the day when what a patient said, and the physician saw and felt, were all that a case of disease had to tell him. The limitations they suffered under, lured or drove them into attempts

¹ Gustav Fischer, Jena, 1913.

² Transactions of the Congress, Vol. II, New Haven, 1892.

to classify, and minutely to multiply the signs of disease, until what they believed they saw and felt represented impossible refinements in symptomatology."

It should be distinctly understood that the operations of the so-called elementary mathematics are not sufficient for the study and the interpretation of natural phenomena and processes. This can be accomplished only by Calculus. In fact, Calculus seems to be the very language of nature. All processes in nature proceed by infinitely small degrees. Consider the growth of a tree or of any organic matter. During the interval of time required to give a glance at the tree, the tree has either grown or decayed. While this growth or decay is so small that it cannot be measured by the most delicate instruments, yet it is as definite a quantity as any finite quantity is. The growth of a tree during a month or a year is made up of the infinitely large number of the infinitely small growths during the infinitely small periods of time. Again, a vessel of water is heated. The infinitely small increase in the temperature of the water is not the same for the different infinitely small periods of time. We say the amount of growth during the different infinitely small periods of time varies. Now these infinitely small numbers which represent the infinitely small increases can be compared with each other just as finite numbers can be compared. The infinitely small increase in the temperature of the water during one infinitely small period of time might be any number of times as large as the infinitely small increase during the same or a different infinitely small period of time.

Also, just as the infinitely small quantities can be compared with each other, so can infinitely large quantities be compared. One infinitely large quantity might be a number of times larger or smaller than another infinitely large quantity. If a piece of material be divided into a number of parts and each part divided again, and if we imagine this division continued until each particle is so small that it cannot be detected by the most powerful microscope, then no matter how far the division is carried on, the particles, although infinitely small, have a definite extension and weight. The sum of the infinitely large number of the infinitely small particles make up the original piece of material. The infinitely large number representing the number of infinitely small particles at one stage of the division might be many times larger or even infinitely times as large as the infinitely large number representing the number of infinitely small particles at another stage of the division. For the term infinitely small the term infinitesimal is used.

The operations of Calculus enable us to study a process during a given period of time by means of the changes which are taking place during the infinitely small intervals of time.

Calculus is divided into two branches, the Differential and the

Integral Calculus. In the first, problems relating to infinitesimal changes are studied and in the second, problems leading to the sum of an infinite number of infinitesimals are considered. Thus: If a body is being heated at a certain rate of increase of temperature, its rate of expansion at any instant may be obtained by means of Differential Calculus. Or again, if a particle moves under the action of certain forces its velocity at any instant can be determined by Differential Calculus and the distance travelled by Integral Calculus.

Helmholtz, the inventor of the ophthalmoscope, who is as well known to the mathematician and physicist as he is to the physician, was led to the results in mathematics from the observation of nature. Professor Leo Königsberger of Heidelberg³ says of Helmholtz: "He obtained his mathematical problems—this is certainly the only true way, but also one to be pursued by so great a master—directly from observation of nature. . . . On this account there is to be found in all his works a great many results, which are interesting even from a purely mathematical point of view, but which uncover deep and intelligible natural laws." By purely mathematical investigation based upon known natural laws, new laws have been derived which have predicted phenomena, which in turn have been verified by observation and experiment. To show what mathematics is capable of accomplishing and what might be expected of this powerful instrument if applied to the study of the human body, I cite the following instances:

One of the most remarkable discoveries in Physics—the law of conical refraction—was made as the direct result of mathematical investigation.

By means of Calculus Sir William Rowen Hamilton found that a point, when looked at through a crystalline place cut in a certain direction, ought to appear not as a point but as a ring. Lloyd, of Dublin, verified Hamilton's results experimentally.⁴

As a direct result of mathematical analysis, Professor Michael I. Pupin, of Columbia University, has invented a process which has considerably increased the distance of communication by telephone.⁵

The discovery of wireless telegraphy owes its inception to mathematics.

The old idea was that electricity could be transmitted from one place to another only by means of metallic conductors, such as wires, etc. The air was considered an insulator or non-conductor of electricity. James Clerk Maxwell, by purely mathematical deductions, arrived at the conclusion that electricity, like light, is

³ Herman von Helmholtz's *Untersuchungen über die Grundlagen der Mathematik and Mechanik*, 1896, p. 2.

⁴ Humphrey Lloyd, *Elementary Treatise on the Wave Theory of Light*, Third Edition, p. 209, London, 1873.

⁵ The Electric Review, Vol. XL, No. 2, 1902, p. 53.

propagated by ether vibrations; that light, radiation and electric radiation are essentially the same and that electro-magnetic waves obey all the laws of optics. A full development of the subject is given in his work, "A Treatise on Electricity and Magnetism," first published in 1873.⁶

As Maxwell's results were opposed to the accepted views, and as his theories were only the result of mathematical deductions the most eminent men of science doubted their validity. Maxwell⁷ himself said: "There appears to be in the minds of these eminent men some prejudice or *a priori* objection, against the hypothesis of a medium, in which the phenomena of radiation of light and heat and the electric actions at a distance, take place." Even Heinrich Hertz⁸ (1857-1894), who ultimately became the champion of Maxwell's mathematical theories of electricity, said: "Notwithstanding the greatest admiration I hold for Maxwell's mathematical conceptions, I have not always felt quite certain of having grasped the physical significance of his statements."

In 1879, the Berlin Academy of Sciences offered a prize for a problem which practically meant the experimental verification of Maxwell's electro-magnetic theory. Hertz took up the problem and succeeded in verifying experimentally Maxwell's mathematical theories. It was, therefore, through mathematics that the so-called Hertzian waves were discovered which Marconi has made use of so ingeniously in connection with one of the most wonderful practical inventions that has ever astonished mankind.

Dr. F. H. Garrison,⁹ in an admirable contribution, says: "Most of the working theorems of modern physical chemistry were stated *a priori* as mathematical consequences of the second law of Thermodynamics by Gibbs, many years before they were actually tried out, and in some cases, rediscovered in the laboratory."

Fresnel¹⁰ (Fresnel's wave surface), in a letter to Young, said: "Without doubt I have often wanted the spur of vanity to excite me to pursue my researches in moments of disgust and discouragement. But all the complements which I have received from Arago, Laplace, etc., never gave me so much pleasure as the discovery of a theoretical truth or the confirmation of a calculation by experiment."

Mathematicians planted the first seeds of accurate and scientific medicine, but unfortunately for the science it was at a time when the sciences of physics and chemistry were only about to spring into being, when the law of gravitation was not as yet established, when Calculus was not yet invented.

⁶ Clarendon Press, Oxford.

⁷ Ibid., Vol. II, third edition, p. 492, 1892.

⁸ Electric Waves, London, 1893, p. 20.

⁹ Physiology and the Second Law of Thermodynamics, New York Medical Journal, Vol. XC p. 494.

¹⁰ Peacock. Life of Young.

René Descartes (born in France in 1596, died in Stockholm in 1650), the inventor of the analytic geometry, was an accomplished physicist. He wrote a treatise on physiology entitled *L'Homme* (1662), which is said to be the first physiology published. Sir M. Foster,¹¹ speaking of the book, says: "But his main idea, that the problems of man ought to be treated in the same way as the problems of the rest of nature, made itself felt and produced effects in after times."

Giovanni Alphonso Borelli (born at Naples in 1608, died 1679), was one of the leading mathematicians and physicists of his day. Under him the University of Pisa became the most famous school for mathematics and medicine. The new methods of physical mathematical research led him to the study of the mechanism of the human body, which he has incorporated in a treatise on animal motion *De motu animalium*. In the preface of the book he states that his purpose in science is "to ornament it and enrich it by mathematical demonstrations."

Both Descartes and Borelli were inspired in their work by the teachings and writings of Galileo (born at Pisa in 1564, died 1642). When Professor of Mathematics at the University of Pisa, Galileo invented the thermometer or thermoscope. It is said that when Galileo was but eighteen years of age and a student in medicine, when sitting in the Cathedral of Pisa his attention was drawn to a huge swinging lamp, which still hangs there. He noticed, that whether the arc through which the lamp swung was large or small, the oscillations occupied the same interval of time. That observation led him to the invention of the pulsilogon, which, though imperfect, was hailed with wonder and delight by the physicians of the day, and was soon taken into general use."¹²

Molecular force has placed each particle of which the bones, the nerves, and the muscles are made up, in its proper place. Speaking of the molecules which make up the human body, John Tyndall¹³ says: "Unless the existence of law be denied and the element of caprice be introduced, we must conclude that, given the relation of any molecule of the body to its environment, its position in the body might be determined mathematically." Mathematics might perhaps help us to discover the laws which govern the changes that take place in the cells and tissues of the human organism, and enable us to direct and redirect these changes. To understand the vital organism of the blood and to determine the blood pressure and the velocity of the blood current in the arteries and veins, a knowledge of the physical-mathematical laws of hydro-dynamics is necessary. The mechanism of labor in normal births is a physical process based on mechanical mathematical principles.

¹¹ Lectures on the History of Physiology, Cambridge, 1901, p. 62.

¹² Viviani. Vita di Galileo.

¹³ Scientific Limit of the Imagination, London, 1870, p. 61.

Ophthalmology, the science of the structure, functions, and diseases of the eye, may be justly considered a branch of applied mathematics. A. Gullstrand of the Medical Faculty of the University of Upsala won, in 1912, the Nobel Prize for his work on the internal mechanism of accommodation to which he applies the operations of Calculus. It is of interest to note that in the Medical Department of the University of Berlin, Professor Gutzmann is giving, during this Winter-Semester, a course in *Mathematische Analyse normaler und pathologischer Sprachklänge*.

The human skeleton, including the various articulations, is constructed in strict accordance with mathematical laws. When the end of a long bone, say the femur, is examined, it is found to be made up of interlacing osseous plates, technically called "concelli." Professor J. Engel,¹⁴ of Prague, says: "Not without a purpose does the structure seem to differ in the various arches, the use here of vertical columns, there of oblique abutments, is certainly intended for something else than to merely delight the eye of the anatomist by pretty carvings." Professor Herman von Meyer, of Zurich, in 1867, presented before the Naturforscher Gesellschaft some specimens which were to demonstrate the inner structure of the human thigh bone. Culman, the founder of graphical statics, who happened to be present, recognized at once in the course and in the arrangement of the concelli, the trajectories of graphical statics, and he was greatly surprised at the similarity between the mysterious workings of nature and the mode of construction followed by scientific engineers. The subject of the construction of bones was next taken up by Professor Wolff, of Berlin, a man combining a thorough training as a physician with a rare knowledge and understanding of mathematics, and who was advised and aided in his work by Culman himself. He has embodied the result of his twenty years' investigation in a work, entitled, "The Law of the Transformation of Bones,"¹⁵ which is interesting alike to the physician, the engineer, and the mathematician. He found that the shape and inner structure of a bone depended upon the direction and the amount of the stress acting upon it, and that changes in the stress will cause definite changes in the form and the structure of the bone, in accordance with strict mathematical laws. And just as a pathological stress will cause abnormal changes in a bone, so, on the other hand, a deformed bone may be made to return to its normal state by well-directed changes in the stress acting upon it. These principles Wolff has made the basis of a new method of the treatment of various deformities of bones, notably club-foot, without resorting to operative measures.

¹⁴ Sitzungsberichte der Wiener Akademie der Wissenschaften, 1851.

¹⁵ Julius Wolff, Das Gesetz der Transformation der Knochen, Berlin, 1892

It would appear that the present generation of physicians are not in a position to follow ideas in the medical sciences if they are represented by means of mechanical-mathematical principles. On that account, investigators of the medical sciences along mechanical-mathematical lines are often obliged to give the results of their investigations without the method by which they have arrived at their conclusion.

The discoveries of Zuppinger in the treatment of fractures of bones is based on mechanical-mathematical considerations. Dr. Th. Christen has embodied Zuppinger's discoveries in a book,¹⁶ from the preface of which I quote the following:

"Right here an objection which we meet at every turn, that Zuppinger's ideas may be very interesting, perhaps even theoretically correct, but that they are too 'mathematical,' too 'abstract,' and not intelligible to the medical fraternity, must be answered. . . . We have, however, owing to the sentiment at present prevailing among our colleagues of the medical profession, made it our duty to keep the principal part of the text of this book free from every mathematical formula. . . . In fact a large number of therapeutical errors which are still taught and practised are based on wrong mechanical conceptions. . . . To give only an approximate idea of the importance of every improvement in this field of science it may be stated that (according to Hoffa) about two-thirds of the premiums paid in workmen's compensation insurance in Germany are the result of poorly healed fractures of bones."

In the preface to his masterly work,¹⁷ written "in erster Linie für Mediziner und Zoologen," Otto Fischer states that he has endeavored to derive and represent the kinematic principles in an elementary way, so that the book may be more generally understood, but in Chapters IV and VI he was obliged to take recourse to the Differential and Integral Calculus, because without it he could not obtain the principles sufficiently general and intact.

Dr. Friedrich von Müller, Professor of Medicine in the University of Munich, on November 17, 1909, addressed the Medical Society of Munich on the topic, "Welche Mittelschulvorbildung ist für das Studium der Medizin wünschenswerth?" The address and the discussion appears in the *Münchener medizinischen Wochenschrift*, 1910, No. 19. To make it accessible to a larger circle of readers it has been published in 1911 in pamphlet form by B. G. Teubner in Leipzig. I quote from it the following:

"If, therefore, physics is to be taught in our universities in such a way as the physicians shall need it later in life, an absolutely different fundamental view must be taken, and this is possible

¹⁶ Allgemeine Lehre von den Knochenbrüchen, Leipzig, 1913.

¹⁷ Die Kinematik organischer Gelenke, Braunschweig, 1907.

only when a higher degree of mathematical knowledge is assumed. Today, not only for the study of physics, but also for the study of chemistry and physiology, a thorough mathematical knowledge is necessary. Physical chemistry which has found numerous applications in medicine and which has become indispensable in our laboratories, assumes a knowledge of higher mathematics. The text-book on physical chemistry by Nernst is for this reason unintelligible to me and, indeed, to most of my pupils. For the same reason I can follow only in part even the text-book for physicians on osmotic pressure and the theory of ions written by Hamburger. There are many students of medicine to whom the important works of Otto Frank on the problems of the circulation of the blood are only in part intelligible, because they presuppose a knowledge of higher mathematics."

During the last few years a great advance has taken place in the x -ray treatment of gynecological diseases and deep cancers, so-called deep treatment. This was made possible by inventing exact instruments for measuring the penetration and the dosage of administered rays. These instruments owe their inception to Calculus.¹⁸

Christen's results in the x -ray treatment relating to high penetration by hard tubes, which he has obtained by means of higher mathematics, have been verified by the practical and experimental work of the radiologists and gynecologists.

The invention and the improvement of some of the instruments used in diagnosis like the manometer, sphygmograph, etc., has been helped by the Calculus and even by its most advanced branches (Differential Equations).

It is an unfortunate peculiarity of the science of mathematics that, while a fair knowledge of one of its special branches might enable the student to follow intelligently the solutions of the simpler problems in this branch, yet even an intimate knowledge of that branch might not enable him to understand in the least degree the results in another branch. The ideas represented by the one branch and the symbolism in which these ideas are expressed are wholly different from the ideas and symbolism of another branch. On that account a specific example illustrating the application of mathematics to any branch of science can only be followed by those who have a knowledge of this branch of mathematics. Those readers who are familiar with the processes of Calculus are referred to the books and articles on the Medical Sciences named below, in which Calculus is applied. These together with the books and articles mentioned in this paper are those to

¹⁸ Th. Christen, Messung und Dosierung der Röntgenstrahlen, *Ergänzungsband 28* of the Fortschritte auf dem Gebiete der Röntgenstrahlen, Hamburg, 1913.

which I had access and the list, therefore, is quite necessarily limited.¹⁹

There are investigators in the medical sciences whose work involve principles of mechanics, which in turn are based on mathematical analysis. To this class of investigators belong I. Traube, of Charlottenburg, M. Ascoli, of Pavia, A. E. Taylor, of Philadelphia, H. Zuppinger, of Basel, L. Bürker, of Tübingen, L. Asher, of Bern, S. Garten, of Leipzig, H. Sellheim, of Freiburg, E. Münzer, of Prag, R. Tigerstedt, of Helsingfors, Ch. Bouchard, of Paris, R. Höber, of Kiel.

How Professor Traube has been helped by the results of physical mathematical investigations in his work on the relation of surface-tension to osmosis, digestion, narcosis, hemolysis, sero-diagnosis, etc., may be judged from the following statement made by him:²⁰ "I attribute the clarification of my views to the fact that my attention was called to an important theorem of which I had not previously been aware, the thermodynamic demonstration of which is originally due to the great mathematical physicist Willard Gibbs."

¹⁹ Th. Christen, Neue Wege in der Pulsdiagnostik, Zeitschrift für klinische Medizin, Vol. 71, 1910, pp. 390 to 401.

O. Frank, Endliche Ausbauchungen einer aufgespannten elastischen Membran, Zeitschr. für Biol., Vol. 50, 1908, p. 281.

S. A. Arrhenius, Immunochemistry, 1907.

K. Hürthle, Experimentalkritik der Frank'schen Theorie der elastischen Manometer, Pflüger's Archiv, Vol. 137, 1910-11, p. 153.

C. Schaefer, *ibid.*, pp. 250 to 258.

J. Wolff, Ueber die normale und pathologische Architectur der Knochen., Arch. Path., Anat., Physiol., 1901.

W. B. Hardy, Physiological articles in the Proceedings of the Royal Society, Vols. 86-88, 1911-1913.

O. Fischer, Physiologische Mechanik, in Encyklopaedie der Mathematischen Wissenschaften, Vol. IV, 1, II, Heft 1, 62 to 126, Leipzig, 1904. The index on the literature of the subject contains a list of 21 text-books and treatises and 421 monographs.

O. Frank, Prinzipien der graphischen Registrierung, Zeitschrift für Biologie, Vol. 53, 1910, pp. 429 to 456.

Th. Christen, Ueber die Anwendung zweier physikalischer Gesetze auf den Blutkreislauf, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VII, 1910, p. 783.

O. Frank, Kritik der elastischen Manometer, Zeitschrift für Biologie, Vol. 54, 1903, p. 445.

K. Hürthle, Betrachtungen über die theoretischen und praktischen Bestrebungen, Instrumente zur Registrierung der im Kreislauf auftretenden Druckschwankungen herzustellen. Pflüger's Archiv für die gesammte Physiologie, Vol. 137, 1911, pp. 145 to 152.

O. Frank, Dynamik der Membranmanometer und der Lufttransmission, Zeitschrift für Biologie, Vol. 50, 1908, p. 309.

I. Petter, Die Leistungen des Sphygmographen. Zeitschrift für Biologie, Vol. 51, 1908, p. 335.

O. Frank, Prinzipien der Konstruktion von Schreibleibern, Zeitschrift für Biologie, Vol. 45, 1904, p. 480.

H. von Recklinghausen: Was wir durch die Pulsdruckkurve and durch Pulsdruckamplitude über den grossen Kreislauf erfahren, Archiv für experimentelle Pathologie und Pharmakologie, Vol. 56, p. 1.

Th. Christen, Die Pulsdiagnostik auf mathematisch-physikalischer Grundlage, Zeitschrift für experimentelle Pathologie und Therapie, Vol. VI, 1909, pp. 125 to 170.

H. J. Hamburger, Osmotischer Druck und Ionenlehre in den medizinischen Wissenschaften, 3 Vols., 1902-04.

²⁰ Pflüger's Archiv, Vol. 132, 1910, p. 511.

The great progress of the technical sciences during the last few decades is to a large extent due to the support it has received from mathematics. No one is taking up the study of the technical sciences without a more or less extended mathematical equipment. But to the study and investigation of the medical sciences, so far only a few have brought a deeper mathematical knowledge, and it is, therefore, the more surprising to learn how these few representatives have in a comparatively short time done so much toward advancing the medical sciences along mathematical lines. It augurs well for the adaptability of the medical sciences to mathematical interpretation and investigation and encourages the hope that, with the increase in the number of investigators with mathematical training and ability, a more intimate knowledge of the organic laws governing the human body will be obtained and a corresponding increase in the efficiency of the methods for curing its ailments will result. While there is no medical school in this country or in Europe, which, as far as I could find, requires of its medical students a knowledge of the Calculus, there are many universities in Europe in which a course in Calculus is offered for natural sciences and medical students. In the Department of Chemistry in the University of Pennsylvania a few years ago a course in Calculus was made obligatory with all students.

The rapid increase during the last few decades in things material which has brought about abrupt changes in all aspects of life, is pressing also for sweeping changes in the fundamental principles of education. There is a tendency to reduce both in school and college, the amount of required mathematics. It is a fortunate circumstance, however, that we have among us men of high educational ideals with a knowledge of the past and a clear understanding of the requirements of the future, who are stemming the tide and saving as much as possible of our educational heritage, until an adjustment of the new conditions will bring those who are carried with the current to the realization and to a sober view of what comprises true education, true progress, and true happiness. The Provost of the University of Pennsylvania, with a deep knowledge of the history of the sciences and of his own specialty, an ardent investigator, with broad sympathies for the needs of those who are to be leaders, is in favor of a curriculum for a liberal education to include a thorough course in mathematics and in the ancient languages. While mathematics still possesses the educational powers as it did at that time of Gauss who found the main charm of the science in its *utter inutil-ity*, it has during the last few decades turned into a subject of *indispensable utility*, not only in the study of the technical sciences, but also in the study of the natural and allied sciences.

A CLINICAL NOTE ON FIBROMA MOLLUSCUM GRAVIDARUM.

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IN 1906, Brickner,¹ described an unusual type of fibroma molluscum in which the lesions developed during early pregnancy and disappeared spontaneously, without scarring, a few weeks after delivery. Brickner's conclusions were based on a study of nine cases of the disorder. One of his patients had had acne vulgaris and one molluscum contagiosum; the cutaneous histories of the other seven were negative. The eruption, which consisted of forty or more small, pigmented or non-pigmented sessile or pedunculated tumors, was asymmetrically distributed over the neck and chest, and the individual lesions were apparently clinically and histologically identical with those found in an ordinary case of fibroma molluscum. The tumors varied in size from a pinhead to a split pea, and gave rise to no subjective symptoms. There was no evidence of thyroid change, and the blood and urine were normal. Brickner considered the disorder as probably metabolic in origin, and suggested for it the name of fibroma molluscum gravidarum.

DeLee² reported a well-defined example of the disease to the Chicago Gynecological Society, in 1908, and Goth's³ case also was probably one of this disorder. Both Buhlig, who examined one of the tumors from DeLee's patient, and Goth found the lesions to be supplied with unusually large numbers of bloodvessels, the tumors differing in this respect from those described by Brickner.

In 1911, Hirst⁴ reported a case of fibroma molluscum in a woman, aged thirty-eight years, a VII-para, in which the tumors had increased in number with each succeeding pregnancy, but had failed to disappear during parturition.

Ward's⁵ patient, who was afflicted with "multiple warts in pregnancy," probably suffered from Brickner's disease, if one may intelligently judge from the meager description given.

Recently, Brickner⁶ in a second communication, added seven more cases to those already reported, and also briefly reviewed some of the contributions of other writers on the subject.

Although small tumors similar to those described by Brickner are not unusual in women who have borne children, I have en-

¹ Amer. Jour. Obst., 1906, p. 191.² Monats. f. Geburts. u. Gynäk., 1908, xxviii, 423.³ Amer. Jour. Obst., 1911, p. 256.⁴ Amer. Jour. Dermat., 1912, p. 240.⁵ Surg., Gynec., and Obst., 1908, p. 204.⁶ British Jour. Dermat., 1913, p. 153.

countered but one case in which the growths followed the characteristic clinical course of fibroma molluscum gravidarum.

The patient was a housewife, aged thirty-eight years, a native of Illinois, and a resident of Galva, Kansas. She was referred to me through the courtesy of Dr. Arthur E. Hertzler, of this city, who had been consulted regarding her condition by the family physician, Dr. Loius A. Bradbury, of Galva.

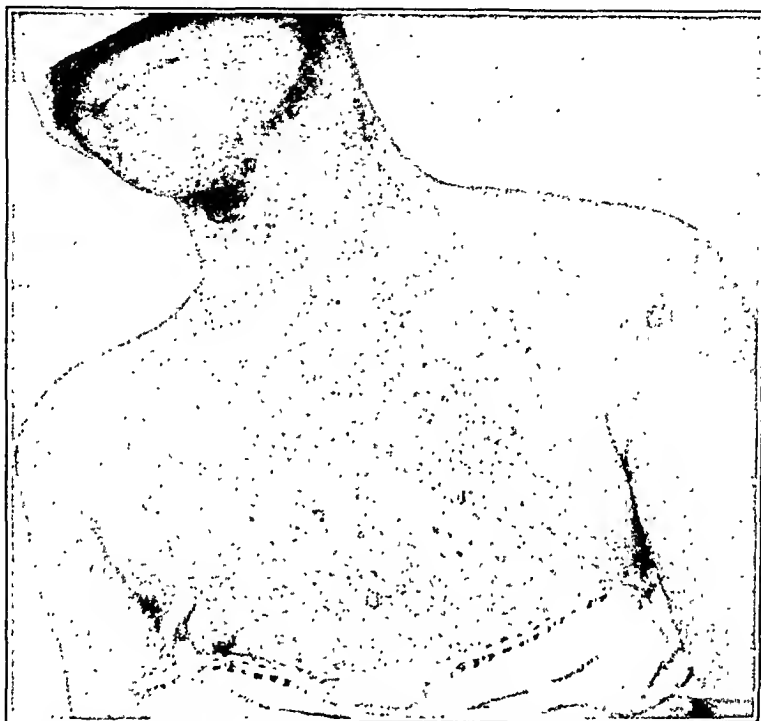


FIG. 1.—Fibroma molluscum gravidarum (case here reported).

The cutaneous history of the family was negative. The patient was a brunette, with a smooth, olive skin, and brown hair and eyes. In intelligence she was above the average, a somewhat unusual occurrence in individuals having well-marked cases of fibroma molluscum. She was the mother of two children, one three years of age and the other fourteen months. Early in her first pregnancy a number, twenty or more, of small, brown pigmented, pedunculated tumors suddenly appeared on her chest and neck. Only the mammary, supramammary, and anterior cervical regions were involved, and the growths gave rise to no subjective symptoms. Shortly after delivery the growths shrivelled and decreased in size, and in the course of three months completely disappeared, leaving no trace. During the second pregnancy another crop of the little tumors developed, some of the lesions being of considerable size, as large or larger than a split pea, and all more or less pigmented. After parturition a few of them

disappeared, but many did not, and it was for relief from those that persisted that advice was sought.

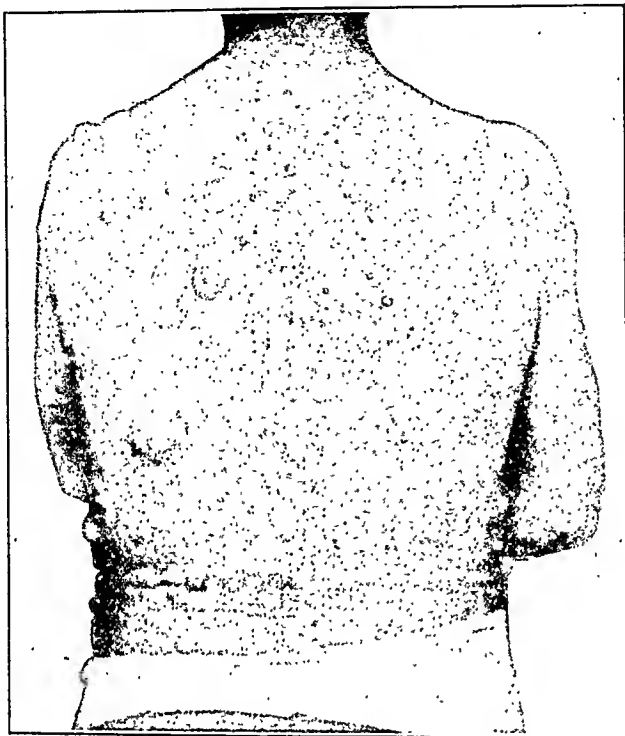


FIG. 2.—Fibroma molluscum of the usual type. The majority of the tumors have been present since the patient's boyhood.

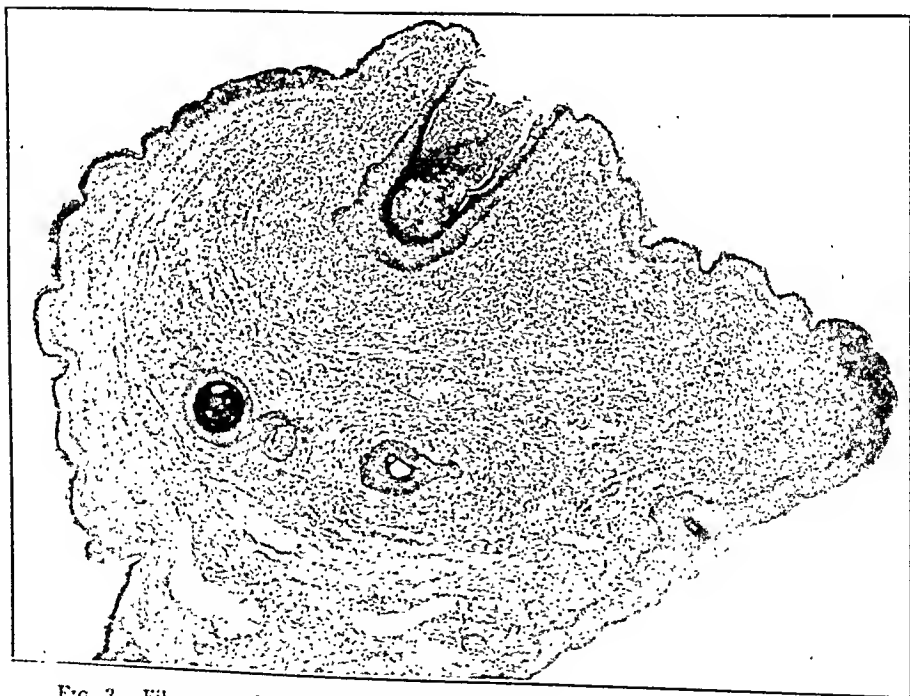


FIG. 3.—Fibroma molluscum of the usual type. Lesion from the case here shown.

A thorough physical examination revealed nothing abnormal with regard to the internal organs. Scattered irregularly over the anterior surface of the chest and neck were a number of the small, round or oval, smooth, soft, pigmented growths characteristic of fibroma molluscum. In addition to these tumors of the usual type there were a half-hundred or more minute, teat-like projections of skin which the patient stated marked the sites of former pedunculated growths, the mushroom-like tops of which had shrivelled and dropped off during the past year. For microscopic study one of the medium-sized tumors, about the diameter of a grain of wheat, was excised under cocaine anesthesia, fixed in formalin solution, mounted in celloidin, sectioned, and stained by the usual methods. The stratum corneum was unchanged.

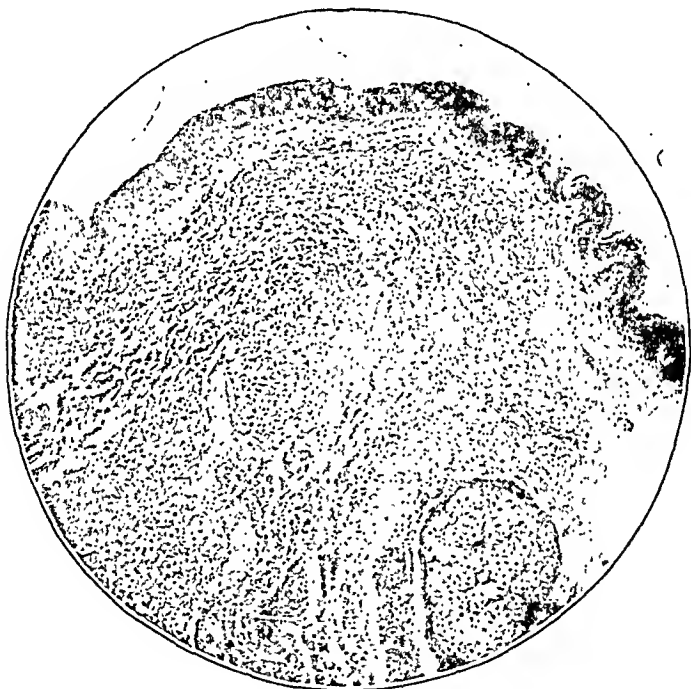


FIG. 4.—Fibroma molluscum gravidarum, showing bloodvessels and newly formed connective tissue in corium, anemic layer, which represents old corium, in papillary and subpapillary regions, and atrophy and pigmentation of rete (moderate magnification).

The granular layer averaged two cells in depth, and the elements were well preserved. The rete was decreased in thickness, deeply pigmented, and the component cells stained deeply and unevenly. The papillae were flattened and the intrapapillary vessels were much diminished in size. The new growth occupied the centre of the tumor, and consisted of newly formed connective tissue, with its accompanying nerves and capillaries. Overlying this central mass, and separating it from the epidermis was a thin stratum of old connective tissue, anemic from pressure, and com-

paratively free from nuelei. In the vicintiy of the dividing line the lymphatics were widely dilated. No mast cells of the type described by Unna⁷ as occurring in neurofibromas⁸ were found. Histologically the tumor was almost a duplicate of the one examined by Goth⁹.

CONCLUSION. The lesions of fibroma molluscum gravidarum are histologically identical with those of fibroma molluscum (the neurofibromas of v. Recklinghausen). As Pusey¹⁰ has suggested, this group of cases demonstrates the possibility of production of fibromata by systemic causes, but as to the nature of these causes we are hardly in position even to surmise.

THE METABOLISM, PREVENTION, AND SUCCESSFUL TREATMENT OF RHEUMATOID ARTHRITIS: SECOND CONTRIBUTION.

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(Concluded from February, 1914.)

TESTS OF KIDNEY ELIMINATION BY MEANS OF PHENOL-SULPHONE-PHTHALEIN.

The tests below were conducted aceeding to the accepted technique of Rowntree and Gerarghty, and need no description here.

CASE VII.—December 22, 1912. First appearance of the drug in four and a half minutes.

At the end of the first hour the elimination was	53.07 per cent.
At the end of the second hour the elimination was	13.72 "
Total elimination was	66.79 "

CASE VIII.—First appearance of the drug in nine minutes.

EXPERIMENT 1.

At the end of the first hour the elimination was	45.00 per cent.
At the end of the second hour it was too dilute to be read	

First appearance of the drug in five minutes.

⁷ Histopathology of the Diseases of the Skin, Walker's translation, New York, 1896, p. 847.

⁸ See v. Recklinghausen, Ueber die multiplen Fibrome der Haut, und ihre beziehung zu dem multiplen Neuromen, Berlin, 1882.

⁹ Loc. cit.

¹⁰ Principles and Practice of Dermatology, New York, 1911, p. 863.

EXPERIMENT 2.

At the end of the first hour the elimination was	40.32	per cent.
At the end of the second hour the elimination was	15.00	"
	<hr/>	
Total elimination was	55.32	"

CASE IX.—First appearance of the drug in ten minutes.

At the end of the first hour the elimination was	37.40	per cent.
At the end of the second hour the elimination was	23.80	"
	<hr/>	
Total elimination was	61.20	"

CASE XI.—First appearance of the drug in seven minutes.

EXPERIMENT 1, MARCH 25, 1913.

At the end of the first hour the elimination was	31.25	per cent.
At the end of the second hour the elimination was	13.22	"
	<hr/>	
Total elimination was	44.47	"

First appearance of the drug in eight minutes.

EXPERIMENT 2, MARCH 27, 1913.

At the end of the first hour the elimination was	33.50	per cent.
At the end of the second hour the elimination was	11.80	"
	<hr/>	
Total elimination was	45.30	"

CASE XIII.—First appearance of the drug in eleven minutes.

EXPERIMENT 1.

At the end of the first hour the elimination was	36.10	per cent.
At the end of the second hour the elimination was	10.20	"
	<hr/>	
Total elimination was	46.30	"

First appearance of the drug in eight minutes.

EXPERIMENT 2, APRIL 19, 1913.

At the end of the first hour the elimination was	43.00	per cent.
At the end of the second hour the elimination was	7.30	"
	<hr/>	
Total elimination was	50.30	"

CASE XIX.—Referred by Dr. F. H. Klaer. This patient's condition was far advanced and he was definitely crippled. The disease was of many years' standing. He was not treated, as he refused to be put on a diet, and left the hospital. It is interesting to note that in the search for foci of infection, this man had had his tonsils and adenoids removed and so many carious teeth pulled that he could eat only liquid and semiliquid diet. No relief followed. Unfortunately, the actual figures of kidney elimination were mislaid, but they were entirely normal on two separate occasions.

CASE XII.—First appearance of the drug in seven minutes.

At the end of the first hour the elimination was	53.00 per cent.
At the end of the second hour the elimination was	9.40 "
Total elimination was	<hr/> 62.40 "

A consideration of the above elimination figures shows that a patient with well-advanced rheumatoid arthritis may have normal elimination and that in no case tested was it distinctly low.

Case XI presented about 32 per cent. elimination at the end of the first hour, but this was no great departure from the normal for her age, which was forty-seven years.

ANAPHYLACTIC EXPERIMENTS.—The joint pains and certain other analogies between rheumatoid arthritis and occasional symptoms of anaphylaxis suggested the possibility that rheumatoid arthritis might be caused by some such mechanism, and experiments along this line were undertaken.

In view also of the demonstrable relation to the disease, of proteids and carbohydrates, there was suggested the possibility of the passage through the bowel, in insufficiently altered state, of some of the elements of the proteid molecule of either animal or vegetable source.

If demonstrated the deleterious action of some of the carbohydrate foods, such as rice and potato, could be explained in part on this basis, as some workers have shown that animals can be sensitized to vegetable proteid by being fed therewith.

As a starting point, Case VII, Case VIII, Case XI, and Case XIII were respectively fed two to three soft-cooked eggs (not boiled) on an empty stomach. Two hours later about 200 c.c. blood were withdrawn from a vein of the arm under aseptic precautions and whipped. The resulting supernatant fluid was centrifuged until fairly clear and then injected in various amounts from 2 to 5 c.c. into the peritoneal cavities of guinea-pigs. In the case of Case XI the blood was withdrawn twenty-four hours after ingestion of the eggs.

At a period more than three weeks later these pigs were injected with varying amounts, from 2 to 5 c.c. of a 25 per cent. solution of egg albumen into the jugular vein or (twice) into the peritoneal cavity.

In the presence of heterologous proteid in the circulating blood of the patients fed upon uncooked eggs the guinea-pigs should have become sensitized to this, and should have shown this sensitization by anaphylaxis when injected with egg albumen. No clear anaphylactic phenomena could be detected, however, in any of the pigs.

Thinking that faulty technique on the writer's part, in giving the anaphylactic injections might be responsible for some of the first negative results, the experiments were continued with the help

of Dr. Richard M. Pearce,¹ to whom obligation is due for this and other courtesies. The results of these experiments were also negative, however.

March 10, 1913. 2 P. M. Case VII was given two soft-cooked eggs. Blood was withdrawn from the left arm at 4 P. M. After whipping and centrifuging, 2 c.c. were injected into one pig and 3.5 c.c. into another. Both these pigs were tested, with the help of Dr. Pearce, on April 8, each getting from 3.5 c.c. to 5 c.c. egg albumen solution, with negative results, as above noted.

March 11. The same experiment was performed on Case VIII, who received three raw eggs at 2 P. M. Blood was withdrawn at 4.30 P. M., and 2 c.c. were injected into the abdominal cavities of each of three pigs. One pig died April 2.

April 3. The remaining two pigs were injected intraperitoneally with 5 and 10 c.c. of 25 per cent. egg albumen solution, with no obvious anaphylactic result, one dying thirty-six hours later. The other was tested again by Dr. Pearce on April 8, as above noted, with no result.

March 30. Case XI. Blood was withdrawn at 8 A. M. and injected into three pigs, as above described, in amounts of 3 c.c. in two pigs, and 2 c.c. in one pig. Patient had had no breakfast, and had been fed one egg twenty-four hours previously. The primary purpose of obtaining blood was for determinations of the urea and non-coagulable nitrogen content. Advantage was taken of this opportunity, however, to include experiments by means of anaphylaxis at a longer period after ingestion of egg albumen.

April 19. The above three pigs were tested with 5 c.c. of 25 per cent. egg albumen in salt solution, with entirely negative results.

May 28. At 1 P. M. Case XIII This patient was fed three soft-cooked but unboiled eggs on an empty stomach, having had no other lunch. At 4 P. M. blood was withdrawn and treated as usual. Pigs 1, 2, and 3 were sensitized intraperitoneally with 5.5, 3.5, and 5 c.c. of blood respectively. Pig 1 showed weakness of the hind legs, malaise, and diarrhea, and died in thirty-six hours. The other two were essentially unaffected by the sensitizing injections.

June 19. The two remaining pigs were injected in the jugular with 5 c.c. of 25 per cent. egg albumen salt solution. Pig 3, which had had 5 c.c. of blood as a sensitizing dose, showed no anaphylactic symptoms. Pig 2, however, which had had 3.5 c.c. of blood, showed symptoms suggestive of anaphylaxis. It kicked violently with the left hind foot, continuing this in the form of scratching movements for a few moments, and then showed great collapse. It recovered from this pretty well after five minutes, and in twenty

¹ The technique used is set forth by Richard M. Pearce, M.D., in the Retention of Foreign Proteid by the Kidney, Jour. Exper. Med., 1912, xvi, No. 3.

minutes appeared nearly normal. This was the sole instance in which anything approaching true anaphylaxis was observed. The evidence from these experiments is therefore negative, and while in apparent harmony with the negative results of the blood analyses and certain other data, it must be more extended before positive conclusions can be drawn on this point. It is to be noted that the pig showing evidences of anaphylaxis was sensitized with blood drawn later after ingestion of eggs by the patient (three hours) than in the other cases. The too early withdrawal of blood may have been the source of failure here, and is to be considered in future work. It must be confessed, however that these generally negative results and the manifestly harmful role played in this disease by pure carbohydrate render this line of investigation of doubtful promise in this particular regard.

ANALYSES OF THE UREA AND NON-COAGULABLE NITROGEN IN THE CIRCULATING BLOOD.—There have recently been devised methods which allow of the accurate analysis of small amounts of blood for such substances as urea, uric acid, and the non-coagulable nitrogen.²

Folin and Denis have shown that in renal disease there are marked departures from health, the total non-coagulable nitrogen rising above the normal of about 25 mg. per 100 c.c. of blood to as high as several times that amount or even in some cases to 180 mg. per 100 c.c.

The applicability of these methods to the study of such problems as the present is obvious. An attempt was made to utilize them and analyze the blood of patients with chronic joint disease: (1) to determine any abnormality in the percentage of urea and non-coagulable nitrogen; and (2) to contrast these analyses made during disease with those made after the institution of treatment and convalescence. It was conceivable that though total analyses of ill patients might show no great departure from normal, comparisons made as just indicated might show relative variations of interest. 10 c.c. of blood were withdrawn from a series of cases, as noted, at about 8.30 A.M., before the patients had had breakfast, to avoid the disturbing influences of digestion. This blood was then promptly injected into acetone-free methyl alcohol and treated according to the technique recommended by Folin and Denis.³

² New Methods for a Determination of the Total and Non-protein Nitrogen, Urea, and Ammonia in the Blood, by Otto Folin and W. Denis, *Jour. Biol. Chem.*, June, 1912, xi, No. 5.

³ These analyses were made by Dr. C. B. Farr and Dr. J. H. Austin, who were conducting analogous observations in connection with nephritis and desired samples of normal and pathological blood as controls for their own series. They kindly included the writer's cases among their own careful observations. A duplication of the requisite apparatus and technique seemed unwise until some preliminary observations had indicated its justification, and the writer wishes to express his thanks and appreciation to Drs. Farr and Austin for this courtesy. The Non-protein Nitrogen of the Blood in Nephritis and Allied Conditions, by C. B. Farr and J. H. Austin, *Jour. Med. Research*, August 1, 1912, xviii, No. 2.

The figures yielded were as follows:

	Total non-coagulable nitrogen in mg. per 100 c.c. blood.			Urea in mg. per 100 c.c. blood.		
	Average.			Average.		
Case VIII, patient ill	20.2	21.7	21.0	11.2	12.6	11.9
Case IX. Experiment 1. Patient ill.	27.8	25.7	26.0	14.7	14.5	14.6
Case XI, patient ill	22.6	22.7	22.65	9.3	10.2	9.6
Case IX. Experiment 2. Patient con- valescent	27.0	26.4	26.7	12.8	12.4	12.8
Case XIII, patient ill	21.6	25.5	25.0	12.0	14.2	13.1
Case XII, patient ill	21.4	25.0	21.7	10.4	11.4	10.4

The nitrogen of strictly normal cases averages from 20 to 30 mg. per 100 c.c. blood. The urea figures in strictly normal cases are usually about 50 to 60 per cent. of those for nitrogen, but in disease this percentage runs higher. The urea figures include the preformed NH_3 of the blood, and constitute the so-called ammonia-urea fraction. These results are remarkably close together, and correspond to those found by Folin in perfectly healthy students. General hospital cases without nephritis show much greater variations, the total nitrogen frequently ranging up to 35 and occasionally to 40 or even more. Nephritis cases have been found usually to range above 40 and in some cases, as mentioned, to 180 mg. per 100 c.c. blood.

These figures apparently indicate that the limit of toleration to proteid in rheumatoid arthritis is not due to any "backing up" of nitrogenous matter in the blood. It will be noted that in Case IX there was no important difference between the analyses made during disease and those made during convalescence, both being well within normal limits. Further observations on this point are pending.

These observations are not without significance, as the methods used permit of an accuracy greater than has been previously attainable, and suggest that there is no important change in these blood elements during this disease. Any abnormality present, however, may be too subtle to admit of estimation, and may act by anaphylaxis or some other imponderable means. It is also conceivable that such an abnormality though present in the blood sufficiently to produce and perpetuate the disease may disappear from the blood after a night's fast.

These are more or less theoretic objections, but they should be examined.

The writer was interested to learn from the joint work of Folin, Denis, Fitz and Frothingham⁵ that in experimental uranium nephritis of rabbits the phenol-sulphone-phthalein excretion agreed

⁴ Duplicates bad.

⁵ Fifth Annual Meeting of the American Society for the Advancement of Clinical Investigation, Washington, D. C., May 5, 1913.

with the non-protein nitrogen retention in the blood in that when the former was low, the latter was high and *vice versa*. This corroborates the writer's observations, in which the elimination by the kidney was high and the retention of non-coagulable nitrogen in the blood was low, with the molecular concentration of the urine as shown by Δ also in accord.

Attempts were also made to test the carbohydrate tolerance of these patients in respect to the glycolytic function, and a series of them was fed 100 to 150 grams of glucose on empty stomachs at 8 A.M. The twenty-four hour urines of the respective periods were collected and analyzed for sugar, with negative results. It is plain that the lowered carbohydrate tolerance of these patients is of a nature different from that characteristic of diabetes.

DISCUSSION. A consideration of the observations adduced in this series of cases permits of certain general conclusions and develops a number of points of interest.

In the first place there seems to be no reasonable doubt that the disease rheumatoid arthritis, for which a host of therapeutic measures but no successful therapy has been heretofore advanced except that directed toward a focus of infection, is in most cases amenable to treatment and can apparently be prevented. Apart from the bony changes resulting from long standing disease, and in the sense that the inflammatory process causative of them may be arrested, it seems justifiable to say that in many cases which have not responded to other treatment or to attempts to remove foci of infection the disease is curable. It should be borne in mind that the consequences of long-standing arthritis are so far-reaching that related functions often become perverted, and there may ensue a trail of complications which masks or prevents the best end-results, just as in advanced diabetes, severe or long-standing cases may eventually get beyond practicable metabolic control.

In this series of 17 cases, representing practically all varieties of the disease, none failed to improve and only 3 stopped short of a gratifying convalescence. In the light of later experience it is fair to conclude that in 2 of these cases (Case II and Case IV), which incidentally were well-advanced, the principles of treatment were not pushed far enough. It became later evident that each case was a law unto itself, with a definite metabolic limit of food tolerance which must be reached by reduction before complete results could be achieved. For clinical purposes at least the disease seems to belong in the category with gout and diabetes, in that on the one hand the proteids and on the other hand the carbohydrates can be tolerated and metabolized in certain amounts only. The analogy to gout is not quite complete, since it is the purins more especially which are at fault in the former disease, but it serves as an illustration.

The role of the fats is not quite so clear, though it seems from the experiments made in connection with Case VII and Case XII that they can be borne and successfully used to fatten those individuals whose reduction of food intake has caused much loss of weight. In any event, they are dietetically less important than the carbohydrates and proteids, but their real limit will be considered in later studies. Until further observation and wider experience develop the limitations and possibilities of the measures here outlined, each case must be carefully scrutinized and guarded. Radical changes in diet may be causative of harm unless intelligently watched, and the author urges that no case be treated heedlessly. The issue cannot be forced, and time is required for recovery under even the most favorable circumstances.

The general metabolic limit of tolerance above described may help to explain the greater frequency of the disease in women. Of 21 cases under observation by the writer only 5 were in men.

With the known greater demand which physical activity puts upon caloric intake it is conceivable that men should, as a class, be better able to metabolize a possible surfeit than would women, whose lives are as a whole more sedentary; this is only an hypothesis, however.

Comment should be made on the frequent sensation of well-being which some patients experienced when placed upon the above diets. This was noted in Cases I, V, VI, VII, XIV, XV, and XVIII (the last is not here reported).

The writer does not wish to be interpreted as asserting that rheumatoid arthritis is a purely metabolic disease, since this has not been proved. The weak link in the metabolic chain, if present, has not been found any more than it has in gout, or in some cases of diabetes, but for clinical purposes at least this conception is useful.

Among the interesting points developed in the present series in this connection is the relation of a focus of infection to the incidence and perpetuation of chronic joint disease.

Practically the only real development recently made in the therapeutics of this condition is in the recognition, removal, and vaccine treatment of such foci, steps which have restored many eases to health. Some careful clinicians believe that all cases are due to an infective focus, known or unknown.

If this be true, it places many instances of the disease in the class of those having a hidden and unrecognizable focus, since the examples are legion in which no infection can be found. Many of the present series who responded well to treatment had been searched for years in this connection without success. Therefore it follows either that there is a distinct type of the disease which is due to an error of metabolism or else that cases having a causative but hidden source of infection respond to dietary measures. This last seems unlikely, except in the sense below described.

The evidence here submitted, therefore, substantiates the views of many observers that in a large number of these sufferers the disease is due to an error of metabolism in the widest sense of the word.

In point of fact, as noted in their case histories, Case XI and Case XIII had obvious sources of infection, but notwithstanding this they responded well to dietary treatment.

A logical view of these conditions is that the metabolism in a broad sense is primarily at fault.

In certain of them there may be an unstable metabolic equilibrium which is upset by an intercurrent infection, and the disease thus induced just as a diabetic in relative health may be precipitated into coma and death by bronchitis or la grippe.

The writer makes no postulates on this score and strongly advocates the removal of infection when possible. The fact remains, however, that many cases incurable by attempts to find and remove infection may be returned to health by the above means.

A question which has long interested students of arthritis is the relations and nature of the two generally recognized types, atrophic and hypertrophic arthritis.

There are many clinical and pathological classifications of the disease, and most writers add to the above one or two more, but atrophy and hypertrophy of the joint structures, singly or together, characterize practically all cases of long standing.

In the preliminary x-ray studies of the cases here reported attention was given to this, and while the atrophic process generally predominated, it was practically always accompanied by hypertrophy in greater or less degree.

Inasmuch as both types responded well to the same treatment, it would seem that atrophic and hypertrophic arthritis have much in common etiologically, or are perhaps manifestations of the same process.

The writer has endeavored to formulate some rule or working hypothesis for reducing the food intake in treating these cases, based on the caloric tolerance per pound or kilo of body weight, but has as yet been unable to do so. In general, the recent cases, especially in young subjects, recover upon a larger intake than do those of long standing, so that but little modification may be required to obtain results. The duration of the disease, however, is not necessarily a criterion as to its severity or the difficulty of arresting it (compare Cases VII and Case VIII) but it is important to begin treatment early to obviate the deformities and incidental evils which otherwise result. The writer has found it useful to observe for upward of a week the normal food intake of a given case, from which the caloric level can be approximated. From this as a basis the new diet can be constructed. It is obvious that in a mild case accustomed to a high metabolic level the food intake

need not be reduced to the point necessary where the reverse is true; at least not until trial has shown this to be necessary.

Those cases presenting some soft tissue swelling as well as joint involvement are generally easier of treatment because progress can be observed in the subsidence of tumefaction and the wrinkling of the skin as well as in freer joint motility; whereas those cases presenting chiefly erosions or overgrowth of the non-articular parts of the bones may present little objective evidences of improvement. The subjective evidence of the patient over a considerable period of time, together with the loss of tenderness and limitation in movement, affords the indices in these instances.

A point which requires emphasis is that of the associated tendinous contracture and apparent ankylosis. When the activity of the arthritis *per se* has largely subsided there may come a point when the case seems to "hang fire." This occurred several times in the author's series, and was the source of considerable worry until the independent nature of the trouble was appreciated. It is of course common knowledge that these cases present contractures such as may be seen after fractures, etc., but the extent to which these contractures may simulate the condition causing them is noteworthy. The patient rarely can differentiate the two, and only close study by the observer will reveal the facts.

The appropriate treatment of such contractures is of course orthopedic, and needs no mention here except to say that, practically speaking, this has been almost as hard a question to meet, as the alleviation of the causative arthritis itself.

The long-standing habit of sparing tender joints and the reluctance to move make these convalescent patients unaware at times, of their own potential.

If to this state be added muscular atrophy, from disuse, leaving muscular tissue insufficient to move the part, the patient's quandary can be appreciated. At this point, and indeed at any stage of the disease, the time-honored adjuvants of baking, local rest, aspirin, etc., can be occasionally used, with benefit, provided they do not mask the real progress of the case through misleading temporary effects and so suggest false conclusions.

Some of the experiences here cited indicate that there may be a greater return of function in advanced cases and in apparently ankylosed joints than would seem *a priori* possible, as Case VIII and Case XI illustrate. Certainly the ulnar deviation so characteristic of these sufferers yields markedly, as shown in Case VIII, Case XII, and others. A point to be observed is that the inflammatory exudate around inflamed joints causes a fog in the x-ray picture which lessens and eventually disappears during convalescence. Unfortunately this does not lend itself well to reproduction in print.

Of the various joints susceptible to involvement, it may be said

that the smaller ones, like the fingers, yield before the larger, such as the knees, which are among the last to subside and to acquire freedom of capsular and tendonous movement.

The spine seems also to be quite obdurate when much involved, though the earlier stages, as in Case VIII and Case XIII, where spondylitis was present, clear up entirely.

It should be noted that pain is a feature which may persist until convalescence has been well established, and may shift from point to point even though the process as a whole be subsiding.

In watching the clinical course of these cases and certain others, there has seemed at times to occur an associated neuritis. Because of this and other observations the writer suspects that some of the neuritides belong to this general category and can be alleviated by the same methods. This is not as yet proved, but the hypothesis is worthy of being tested in suitable cases of sciatica, circumflex neuritis, and the like. Case VI illustrated this point, as she had neuritic pains in her arms. To what extent this is true of the ocular manifestations of so-called chronic rheumatism cannot yet be stated, though here again some evidence at hand is suggestive, and a trial should be made.

The relation of acute inflammatory rheumatism to the condition here discussed is interesting and undetermined. The present conception of acute rheumatism is that it is an infectious disease. Whether any other variety exists is not known, but some of the present series manifested phenomena suggestively close, clinically, to the acute form, and the writer has observed at least one case apparently of this type in which the present methods were productive of unusual results. The evidence now at hand seems insufficient for more than hypothesis, but there is at least ground for suspicion that the relation of acute inflammatory rheumatism to chronic rheumatoid arthritis may be in some cases closer than has been thought. This is being made the subject of further investigation.

Much has been written as to the etiological relation of the large bowel to this condition, and in the above cases some attention was directed to it.

Of 17 cases x-rayed the large bowel was elongated, tortuous, and sometimes ptosed in 14. The remaining 3 showed practically a normal position of the large bowel, but, of them, 2 were very constipated. The disease may therefore occur in persons in whom no anatomical abnormality of the large bowel can be demonstrated by the x-ray, as in Case II, Case XV, Case XVIII, not here included, and possibly Case XI.

Constipation seems to be a frequent though in no sense a necessary feature.

The complete role, if any, which the colon plays is not yet elucidated, though it is clear, as pointed out earlier, that proteid putrefaction within the colon is not a factor. Colonic lavage,

active purgation, sour milk dietary and other measures directed to this end, are therefore superfluous, except in so far as the general health may be benefited in other connections. Whether there may be absorbed from the colon noxious products of the break-down of both carbohydrates and proteids cannot be stated, but in any event the process is not that above discussed. The evidence to date is not in favor of the view that the disease is caused in or by the large bowel.

Attention should be called to the low number of calories upon which some of the reported cases subsisted and improved.

Case XI, Case XII, and Case XIV, after an initial fall of weight, nearly maintained an equilibrium upon about 1100 calories, a figure which is somewhat at variance with most clinical teaching as to the low limit permissible.

Sondén and Tiegerstedt, for example,⁶ quote for the minimum figure for metabolism during sleep and as complete rest as possible, 24 to 25 calories per kilo, and in Case XI, here cited, they were about 20.

The above patients suffered no harm during these periods and eventually recovered, but while on the low diets were of course kept in bed. It is obvious that when it becomes necessary greatly to reduce the caloric intake of a severe case the energy output must be reduced as nearly proportionately as possible, to avoid tissue loss. The question of the calorimetry in this connection, however, is a chapter by itself, and may be made the subject of a later contribution. It should be noted that the disease began with all of these patients when they were on full diet and that during this large intake many of them developed the secondary anemia so common to this condition.

The writer is fortunate in that most of the cases cited here have been referred by other physicians, as noted in the text, who were familiar with the previous conditions of the patients or had actually treated them. Their independent observations often served as a useful control of the writer's deductions, and he owes an expression of appreciation for their interest and courtesy.

CONCLUSIONS. 1. Rheumatoid arthritis is apparently a preventable disease.

2. In most instances, except where the general health is undermined by great deformities and sequelæ of long-standing, the disease can be arrested.

3. For clinical purposes at least it seems to belong in the category with diabetes and gout, in that there is in each case a limit of toleration for carbohydrates on the one hand and proteids on the other. The role of the fats is not yet entirely clear, but they may prove to be borne analogously to the carbohydrates and proteids.

⁶ Hammarsten, *Physiological Chemistry*, 1911, 6th ed., p. 878.

4. After arrest of the arthritis the diet can generally be gradually increased until in some cases it differs but little from that of health.

5. Both hypertrophic and atrophic arthritis respond to these measures, and their common etiology seems probable.

6. The presence of an intercurrent or possibly causative infection is not necessarily a contraindication to treatment, and recovery may take place in spite of it, though such factors should be eliminated if possible. *The large group of cases in which a causal source of infection cannot be found or removed lends itself particularly to these measures.*

7. Care is necessary to determine the highest level of metabolic equilibrium at which the arthritis will subside, and at or near that point the patient should be maintained.

8. While the general health improves with the subsidence of the arthritis, and though the patients seem to acquire a toleration for a larger dietary, the general principles above described must be rigidly observed or relapse will occur.

9. The disease is apparently not due to faulty elimination through the bowels or kidneys.

10. It is clearly not due to "intestinal putrefaction" so called. There is no reason to exclude proteid in dietary treatment, except in the sense above described, and the ordinary carbohydrate food-stuffs are also clearly capable of causing the disease.

The writer is indebted for courtesies and assistance which it is difficult properly to acknowledge.

To Dr. Samuel McC. Hamill, whose generous and broad-minded support has greatly increased the opportunities for this work; to Dr. Charles W. Burr; to Dr. William E. Hughes for the use of beds in his wards and other kindnesses; to Dr. W. S. Newcomet for coöperation in the x-ray studies; to Dr. Richard M. Pearce for assistance and advice; to Dr. Francis O. Allen and Dr. J. E. Sweet for surgical help; to Dr. Damon B. Pfeiffer, director of the pathological laboratory, for cordial coöperation. Appreciation should also be expressed to the President and the Board of Managers of the hospital for meeting many of the writer's requests, and to Mr. G. B. Kirkbride, superintendent of the hospital, for his receptive and helpful attitude toward new problems.

REVIEWS

TRAVAUX DE CHIRURGIE ANATOMO-CLINIQUE. By HENRI HARTMANN, Professor in the Faculty of Medicine of Paris, Surgeon to the Biehat Hospital; Member of the Society of Surgery; with the collaboration of B. CUNÉO and PAUL LECÈNE, Adjunct Professors and Surgeons to the Hospitals; KÜSS, Prosector to the Faculty; DELAMARE, V. HENRY, and LEBRETON, sometime Internes in the Hospitals. Fourth Series. Urinary Passages. Pp. 472, with 132 illustrations. Paris: G. Steinheil, 1913.

SEVEN years ago we had the pleasure of reviewing in these columns the third series of these well known Anatomico-Clinical Studies by Hartmann and his pupils. That series dealt with intestinal surgery; in the present series he returns to the urinary system which was studied in the first and second series.

Hartmann has long been recognized as a remarkable man. Claimed as one of themselves by the gynecologists, his work in abdominal surgery, especially that of the stomach, is classical; while his long experience in the *Service Civile* at the Lariboisière Hospital, has marked him as a master of the surgery of the male genito-urinary tract.

The present volume is richly illustrated, and includes a number of important monographs, as well as articles of less magnitude. Küss describes the normal anatomy of the prostate, and Cunéo discusses in most interesting manner the question of the anatomical seat of the lesion commonly called prostatic hypertrophy. The theory he supports, formulated in 1905 by Motz and Péréarnau, is that the lesion occurs not in the prostate at all, but in the sub-urethral glands; and that the change is truly neoplastic in character. This view is steadily gaining ground, and appears to rest on sound reasoning, though all the facts have not yet been proved. This theory renders easy of comprehension the fact of the success of the modern suprapubic operation in cases of adenomatous enlargement, and its unsuitability for cases of urinary obstruction due to other types of prostatic disease.

Hartmann describes in some detail the technique of "transvesical prostatectomy" and, with the aid of Küss, narrates at a length of 87 pages the immediate and remote results of operation in 118 cases of prostatic hypertrophy. This number includes a few cases

of suprapubic cystostomy and of the Bottini operation; 43 operations of perineal prostatectomy; and 61 transvesical operations. Of particular value are the notes of the remote results, and especially the detailed study of specimens secured post-mortem from patients who died long after operation. One cannot admire too much the scientific spirit of the authors which has prompted them to spare no pains to render the case histories as complete as possible.

Other contributions of great value, by Hartmann, are "Some Reflections *à propos* of 47 Operations for Tumors of the Bladder:" a monograph of more than sixty pages on the "Technique and Results of Operations practised on the Kidney;" and one of considerably over 100 pages on "Surgical Treatment of Renal Diseases." Shorter articles of great interest are a "Note on the Histological Lesions in the Kidney Encountered in Certain Cases of Anuria," by Lecène; on "The Presence of Lecithins in Hypernephromas," by Delamare and Lecène; a "Contribution to the Study of the Surgical Treatment of Extrophy of the Bladder," by Cunéo; on "Osseous Foreign Bodies in the Bladder, Especially Sequestra from the Pelvis or Vertebral Column," by Küss; on "Nontuberculous Abscesses of the Prostate," by Hartmann and Lavenant; and on "Gonococcic Abscess of the Prostate," by Lebretton. Nor should we omit to mention the operative statistics of the *Service Civiale* (which form a continuation of the statistics published in the Third Series) extending from 1904 to 1907, the date when Hartmann was transferred from the Lariboisière to the Bichat Hospital.

To produce such a work as this has required an immense amount of painstaking labor; but its authors, and especially Professor Hartmann, who has inspired it all, may rest well assured that this further important contribution to scientific surgery is estimated at its true value by scholarly surgeons throughout the world, and that it has already taken its place as one of the classics of Urology.

A. P. C. A.

PATHOLOGY, GENERAL AND SPECIAL. A MANUAL FOR STUDENTS AND PRACTITIONERS. BY JOHN STENHOUSE, M.A., B.Sc. (Edin.) M.B. (Tor.), formerly demonstrator of Pathology, University of Toronto, Toronto, Canada. Second edition, revised and enlarged; including selected list of State Board Examination Questions. Pp. 287; illustrated. Philadelphia and New York: Lea & Febiger, 1913.

THIS book is a good epitome of the vast subject of pathology. The subject is treated as pathological anatomy, while physiology and theories are omitted. By so doing the author has been able

to compress much into his work. The inclusion of hints as to theories and physiology would help the student in consulting larger books and would occupy very little space, which could be obtained by omitting the chapter on technique, a subject rather too briefly presented to warrant its retention.

The order and system used in larger books have been followed by Stenhouse but at the end of each chapter are printed a number of leading questions upon the preceeding matter. The State Board questions are at the end.

It is not quite clear why the author includes "Internal Secretions" under the endogenous intoxications, as he does not later take up their toxicity. Their absence rather than their presence is toxic.

The eye and ear are not included, one of which at least has quite as important a pathology as the skin.

On the whole, however, the book condenses the complex subject of pathology in a way that should prove highly useful to the student.

H. F.

THE MEDICAL RECORD VISITING LIST FOR 1914. New York: William Wood & Co.

THIS very handy medical day book is spaced in weekly periods throughout the year and makes possible the carrying of sixty names at a time.

Into its brief compass are crowded space for memoranda of all kinds, pregnancy charts, matter on the metric system, drugs, poisons, emergencies, and a short statement of the steps necessary to insure the execution of a valid will.

A. A. H.

PATHOLOGISCHE ANATOMIE: EIN LEHRBUCH FÜR STUDIERENDE UND AERZTE. By L. ASCHOFF, Prof. of Pathology, University of Freiburg, i. Br., Germany. Third Edition. Volume I: General Etiology and Pathology, pp. 811; 431 illustrations. Volume II: pp. 1040; 661 illustrations. Jena: Gustav Fischer, 1913.

THE excellence of this text-book of pathology, edited by Aschoff with the assistance of other German pathologists, is shown by the fact that the third edition has appeared within four years of the first. A comparison of the first (AMER. JOUR. MED. SCI., 1910, cxi, 281) and third editions shows that to the first volumes have been added 175 pages and 67 illustrations and to the second 225 pages and 108 illustrations. This makes both volumes of the present edition rather bulky and unwieldy, but this slight disad-

vantage is forgotten in the general excellence of the text and the great value of the numerous illustrations, an unusually large number of which are colored. The extensive review in these pages (AMER. JOUR. MED. SCI., 1912, cxliv, 276) of the second edition, in view of the fact that no important changes have been made in the present edition, renders unnecessary detailed comment at this time. The book remains the most complete and best illustrated general treatise on pathological anatomy for the use of students and physicians, and as it is representative of the best thought of the present-day German school of pathology cannot be too highly commended.

R. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia, etc., Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. III, September, 1913. Pp. 310; 31 illustrations. Vol. IV, December, 1913. Pp. 411; 70 illustrations. Philadelphia and New York: Lea & Febiger.

THE September number of *Progressive Medicine* begins with an article on diseases of the thorax and its viscera comprising 90 pages, by William Ewart. Over one-half of this contribution is devoted to an admirable and timely discussion of pulmonary tuberculosis. The remaining pages are given over to accounts of interesting features in physical diagnosis, bronchial affections and their treatment, and cardiology and the cardiovascular system. William S. Gottheil contributes a valuable article of 54 pages on dermatology, devoting considerable space to syphilis. Obstetrics is reviewed by Edward P. Davis in an exhaustive summary of 100 pages. Pregnancy, labor, and its complications, embryotomy, and conditions in the newborn are the headings under which he describes many important subjects. The last contribution is on diseases of the nervous system. In 54 pages William G. Spiller, with characteristic care and thoroughness, takes up a large number of interesting topics.

The December number opens with a contribution of 112 pages, by Edward H. Goodman, on diseases of the digestive tract and allied organs. As usual, gastric ulcer and carcinoma claim considerable attention. Duodenal ulcer, peristalsis and anti-peristalsis of the large intestine, the treatment of intestinal toxemia, hepatitis, diseases of the biliary tract, and pancreatic conditions may be noted as a few of the many topics described in this painstaking article. An excellent, but short, contribution of

19 pages by John Rose Bradford, on diseases of the kidneys is followed by a paper of some 48 pages on genito-urinary diseases by Charles W. Boney. Joseph C. Bloodgood again contributes a noteworthy review of 102 pages on the surgery of the extremities, shock, anesthesia, infections, fractures and dislocations, and tumors. The always instructive and practical discussion of therapeutic advances by H. R. M. Landis, occupies 96 pages and concludes the volume.

A survey of the four volumes of *Progressive Medicine* that appeared during 1913 makes it evident that the contributions to this useful quarterly continue each year to be of increased interest by reason of the care and excellent critical judgment displayed in their preparation.

G. M. P.

MANUAL OF TROPICAL MEDICINE. BY CARTELLI and CHALMERS.
Second Edition. Pp. 1747; 630 illustrations. New York:
William Wood & Co., 1913.

IN 1910 the first edition of this work appeared, as a result of studies upon pathological conditions occurring in tropical Africa and Asia. Additions to the first publication (which consisted of 1250 pages) will be found in almost every part of the book and yet the publishers have managed to confine this increase in matter to one, though perhaps rather bulky, volume. It would seem that a future edition would be rendered more serviceable in two volumes, with binding and paper as light as possible. Not infrequently investigators in the tropics go to distant points for study, taking their apparatus and literature. Castellani and Chalmers are the authors, yet it is evident that the most generous aid in text and illustration has been rendered these writers, in the preparation of this work. Among those who have so rendered assistance are Leishman, Ross, Nuttall, Grassi and many other authorities in tropical medicine. The worker in this field is, for the most part a philanthropic scientist and renders without stint or selfish reservation every contribution at his disposal. When, therefore, the second edition of this work appears three years after the first with additional names such as Splendore, Stephens, Brumpt, Newstead, Terni, Mesnil, MacLeod, Pittaluga and many others (34 in all) from whom "kind help" was received, we may feel that the authors have brought together the most valuable opinions obtainable to date. The work omits descriptions of practical laboratory methods and detailed descriptions of bacteria. In place of such descriptions space has been given to parasitology and treatment. Indeed the work may be considered to be, in text and illustration, a treatise on parasites and parasitic diseases. The parasites are physiologically, biologically, and anatomically con-

sidered in detail and diagnosis and treatment of the diseases they produce are dealt with at length. Treatment in general is taken up with such care and thoroughness that these chapters must be given a place among practical works on therapeutic and preventive medicine.

The chapters on tropical races and climatology and effect of food and climate on man in the tropics, present some valuable contributions to the study of the suitability of localities for settlement and of the methods of food supply and preservation.

The sections on the physical and chemical causes of disease contain much valuable information of special as well as of general interest.

Those better qualified than the present reviewer will doubtless find in the work features to adversely criticise, and time too will disclose errors and omissions, but one can not but congratulate the Profession upon obtaining in so small a space the result of so extensive an amount of research work by the world's greatest authorities.

The dedication of this, as well as the first, edition to Sir Patrick Manson, whom the authors entitle "The Founder of Scientific Tropical Medicine," is peculiarly fitting. C. N. B. C.

BLOOD PRESSURE IN GENERAL PRACTICE. By PERCIVAL NICHOLSON, M.D. Pp. 157; 7 illustrations. Philadelphia and London: J. B. Lippincott Company, 1913.

Few subjects in medicine have attracted more widespread attention during the past decade than have studies on blood pressure and its clinical application. As a consequence a voluminous literature has rapidly accumulated and much speculation and controversy has arisen. As the result of these many observations, certain facts of great clinical importance and practical value have been established; but these facts are so scattered through the literature of a number of years that it has been well nigh impossible for many to become familiar with them. Nicholson, appreciating this situation, has been the first since Janeway's memorable book appeared in 1904, to gather together the important and well established facts that have been ascertained in reference to blood pressure. He has written a little book primarily for the general practitioner and student. He has avoided the temptation to digress into the alluring realms of the pathology and physiology of arteriosclerosis, nephritis, etc., has wisely adhered strictly to his purpose and has given us an admirable, concise account of the value and significance of blood pressure determinations in general practice.

After a few pages devoted to general considerations and defini-

tions, he describes the methods of estimating blood pressure. He emphasizes the importance of the auscultatory method, which he rightly regards as the most reliable method and the only simple one which gives accurately the diastolic pressure. Incidentally, his account of how to determine diastolic pressure is correct and in accordance with the most recent observations on this point. He also dispells some of the confusion that has arisen in regard to the inertia of mercury by pointing out that from the practical standpoint it is of little significance.

The second chapter is devoted to a discussion of various blood-pressure instruments. Although admitting the advantage of their portability, Nicholson regards the spring aneroid type of instrument as inaccurate and not dependable. At the close of this chapter, with becoming modesty, he devotes only a little over a page to a description of the admirable sphygmomanometer of his own invention, an instrument which in the hands of many has proved reliable, convenient, and in every respect satisfactory.

It is gratifying to note in a later chapter that this author lays particular stress on the importance and significance of the heretofore too much neglected diastolic pressure and pulse pressure. The subjects of hypertension and hypotension, the conditions in which they occur, and their treatment, are well considered in separate chapters. Blood pressure in surgery and anesthesia and the importance in life insurance are also taken up. A useful, though incomplete bibliography, and a careful index, conclude the book.

The book is written in a way that should make clear to the most inexperienced the fundamental principles upon which blood pressure and its determination is based. Moreover, the practical importance of the subject is pointed out so definitely that this little book should do much toward popularizing sphygmomanometry among those practitioners who have as yet failed to appreciate its inestimable value.

G. M. P.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. II, No. 5, October, 1913; and No. 6, December, 1913. Pp. 175 and 187, with 83 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THESE two numbers of *Murphy's Clinics* conclude the second volume of this remarkable work. It has been a little more carefully edited than the first volume, but there still is much room for improvement. The general plan of the work remains the same, but there has been a freer use than in the first volume of clinical talks and lectures by other teachers than Dr. Murphy, himself,

thus in the October number there is a "talk on cancer" by Dr. W. L. Rodman, of Philadelphia.

Some of the editorial shortcomings may perhaps be alluded to: most notable of all, because appreciable at a glance, is the persistence of Dr. Murphy in using the barbarous phrase "osteitis fibrosa cysticus;" this jumble of Latin genders cannot be attributed to a mere typographical error, because it is so frequently repeated that Dr. Murphy evidently believes it to be correct usage. Another editorial shortcoming is failure to correct and revise crudities of diction; for example (p. 797): "Again it will be noted how the transplanted periosteum remained as a white line for seven months after the implantation, and that it was an apparent detriment to the production of bone;" (this is clear enough, of course, and inculcates an important lesson; but hear what follows): "It was finally involuted by bone formed from the periosteal zone helm at the nail upward around the new-formed callus and outside of the transplanted periosteum." Now, what on earth does all this mean?

Still another editorial shortcoming, rather amusing in its effect, is failure in some instances to harmonize premises with conclusions; for instance: Dr. Murphy is operating on a patient with a healed duodenal ulcer, in whose case no positive diagnosis had been reached before operation; he finds (p. 826) "a strangulating band extending completely across the stomach and constricting it in the pyloric zone." He comments: "All the symptoms which he has had can now be interpreted. He has had blood in his stools. He has had an ulcer here at some time which caused that constriction." Then, *mirabile dictu*, Dr. Murphy adds, a few lines further on, "He did not have a single symptom pointing to this condition." Surely only a genius like Dr. Murphy can explain all the symptoms by the pathological changes when the patient had not a single symptom which pointed to the pathological changes found.

But, all captious criticism aside, even though Dr. Murphy frequently, if unconsciously, contributes to the gaiety of nations (these Clinics are read all over the world), his contributions to surgical diagnosis and technique are of more importance, and are always gratefully received by students everywhere.

A. P. C. A.

COLLECTED PAPERS BY THE STAFF OF ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA, 1912. Pp. 842; 219 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THE Mayo Clinic continues to issue, yearly, a volume replete in interest, valuable for reference, and covering increasingly

various fields of surgical activity. Surgery of the alimentary tract is gradually being overtaken by that of other departments.

Most of the papers are concerned less with operative technique and the immediate mortality of operation (as was formerly the case) than with pathogenesis, diagnosis, and ultimate results. Most of the papers, also, are comparatively short, and in the case of some of those which appear longest, closer investigation shows that most of the bulk is formed by the illustrations. Thus, MacCarty and Blackford contribute a paper of the "Involvement of Regional Lymphatic Glands in Carcinoma of the Stomach," based on a study of 200 specimens obtained at operation; 22 pages of this article are devoted to diagrams of the position of the infected lymph nodes, 5 pages to half-tone illustrations, and only 10 pages to text. C. H. Mayo discusses the "Surgery of the Single and Horseshoe Kidney" in a paper of 15 pages, of which only a little more than half is text; there are 9 figures representing the gross appearances of specimens, only two or three of which seem of real merit. Indeed, it is questionable whether it is ever worth while to publish photographic reproduction of more than a very few pathological gross specimens, since they often appear merely as ink smears even in the best reproductions.

The volume also contains many important articles which have already taken their place in surgical literature, notably those dealing with the surgery of the spleen, of the thymus gland, and on benign and malignant ovarian cysts. At the end are to be found a number of papers and addresses on topics of more or less general interest; and finally a short note on the Laying of the Corner-Stone (October 10, 1912) for the new office, laboratory, and library building in process of erection for the Mayo Clinic. Dr. Mayo said: "The object of this building is to furnish a permanent house wherein scientific investigation can be made into the cause of the diseases which afflict mankind, and wherein every effort shall be made to cure the sick and the suffering. It is the hope of the founders of this building that in its use the high ideals of the medical profession will always be maintained. Within its walls all classes of people, the poor as well as the rich, without regard to color or creed, shall be cared for without discrimination."

A. P. C. A.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Acute Graves' Disease.—In reporting 4 cases of acute Graves' disease, FUNKE (*Zentralbl. f. inn. Med.*, 1913, xxxiv, 705) agrees with Schlesinger and others, that the one most characteristic symptom is tachycardia: exophthalmos and struma are often notably insignificant; other typical manifestations are marked arrhythmia, increased blood pressure, and exceedingly rapid emaciation. Fever of a remittent type is commonly seen. In all cases there was considerable splenic enlargement, intractable vomiting, and more or less continuous jerking of the entire body, reminding one of a chorea major. Dysphagia was frequently complained of. In 1 case there occurred tetany-like cramps in the hand and a positive Chvostek's sign. Jaundice was encountered, and considered to be of toxic origin as was the splenomegaly. Status lymphaticus was present in 2 cases. The usual determining cause of acute Graves' disease is some severe psychic shock. Funk advises against surgical intervention; all 4 cases had a successful outcome, though none were benefited by the use of anti-thyroidin.

Functional Test of the Kidney in Uremia.—FOSTER (*Arch. Int. Med.*, 1913, xii, 452) cites three different types of nephritis for the purpose of emphasizing the importance of functional tests by themselves. The first, with cardiac hypertrophy, arterial hypertension, albuminuria and cylindruria, developed albuminuric retinitis in November. In December, the excretion of phenolsulphonephthalein was 53 per cent. Death in coma occurred suddenly in February after a convulsion. Section showed a red granular kidney. The second case showed no cardiac enlargement or hypertension. There was

albuminuria and cylindruria. The excretion of phenolsulphonephthalein three days before death, while the patient was in coma, amounted to 63 per cent. Section revealed a small granular kidney. The third case was characterized by anasarca, small heart, and low blood pressure, considerable albumin and many casts in the urine. Death was sudden after a convulsion. Eleven days before, the phthalein test gave 57 per cent. output. The clinical diagnosis in last case was confirmed at section. In all the phenolsulphonephthalein test gave a figure approximating normal. Yet in view of the termination of the cases, one would hardly venture to assert that the renal function was normal. As to prognosis, this test would have indicated that recovery was almost certain. Foster questions whether the excretion of this drug does not depend on some other factor than pure renal disease, which by its presence or absence determines the rate of secretion by the kidney—as circulation or non-protein nitrogen in the blood. However, the same finding occurs with incoagulable nitrogen in the blood in uremia. Foster cites a case of death from uremia with a low normal estimation of non-protein nitrogen in the blood. He warns that the consideration of such methods of investigation as ultimate criteria leads into errors of diagnosis, narrowed medicine, and false ideas as to the pathology of a disease entity.

Chemical Nature of Eosinophilic Granules.—MÜLLER (*Wien. klin. Woch.*, 1913, 1025) found that if air-dried blood films are fixed for six hours in the incubator, submerged in a saturated aqueous solution of $K_2M_2O_4$: without washing, then stained for several hours in Kultschitzky's hematoxylin solution and finally counterstained with Weigert's borax-ferrocyanide mixture until the red-blood cells are colorless, and the white cells appear as bright gray disks the eosinophilic granules then appear as brown or blue-black dots. After the action of various lipid solvents the granules will no longer stain black in the above method, though they retain their affinity for acid aniline dyes. This affinity is probably due to a protein complex—as demonstrated by Petry; but besides this, the granules probably are made up of some lipid constituents.

On the Effect of Opiates upon Peristalsis.—E. STIERLIN and N. SCHAPIRO (*München. med. Woch.*, 1913, lix, 2714) find that the x-ray studies of the effects of opium and its derivatives on peristalsis in the stomach and intestines, as reported in literature, are very conflicting. They have therefore, investigated the subject on man and on animals. Patients with fistulæ of the small intestine and with cecal fistulæ, as well as normal individuals have been studied. In a dog the small intestine was divided half-way between the stomach and large bowel. The upper half was implanted in the cecum, whereas the open end of the lower half was inserted in the abdominal wall. By this means it was possible to study the effect of the drug on the stomach and small intestine separately. Stierlin and Schapiro find that morphine has a variable action on gastric peristalsis. Usually in the young, moderate doses delay the emptying of the stomach several hours, even to twice the normal time. In adults, on the other hand, this action is much less marked and less constant. In 2 cases of hyper-

motility of the stomach, the emptying was even more rapid with opium than without it. In the small intestine they found a delay of the intestinal contents under the influence of morphine amounting to as much as seven hours. Often only the lower ileum remained filled longer than the normal time, suggesting a contraction of the sphincter at the ileocecal opening. No alteration could be discovered in the tonus of the small intestine. Upon the large bowel, no affect was observable, opium and pantopon acting in practically the same way as morphine. In chronic diarrhea with marked hypermotility of the small and large intestine, opium produces a slight retardation in the passage of the contents in the lower part of the small intestine; no effect was found on peristalsis of the large bowel down to the sigmoid flexure. The sigmoid remained filled longer than without the morphine. The constipating effect of opiates is due not so much to retardation of peristalsis as to dulling or inhibition of central defecation reflexes and the resulting delay of the contents in the sigmoid, Stierlin and Schapiro conclude.

Diastolic Ferments in the Urine.—(*Deut. Arch. f. klin. Med.*, 1913, iii, 164.) In making determinations of the diastatic ferments in the urine, according to Wohlgemut's method, NEUMANN calls attention to the fact that reliable estimations should be based upon the twenty-four-hour output. The total diastatic ferment amount, *per diem*, varies much with the same individual, and appears to be influenced more by psychic factors than by changes in the diet. Generally the diastatic power of the blood serum is less than that of the urine. This is found to be definitely decreased in diabetes mellitus, the amount of reduction being of some prognostic value. It is also diminished in pernicious anemia, Basedow's disease and in some forms of nephritis. The notable increase in pancreatic disease, is of real diagnostic worth. There is a slight increase in urinary diastase in some febrile conditions. Investigations carried out in a number of other diseases showed no great deviation from the normal.

Experimental Pathology and Therapy of Syphilis.—UHLENHUTH and MULZER (*Arch. a. d. Kais. Gesundh. Amt.*, 1913, xlv, 307) report a long and extensive series of investigations carried on in the field of experimental lues. Human luetic material was used, after numerous passages through dogs, a process which greatly increases the virulence of the spirochete and decreases the incubation time of the disease. Intravenous or intracardiac injections of such material in dogs, causes, in a high percentage of cases, generalized lues. In from six to ten weeks the animals become unkempt and lean. Soon there appear, especially in young animals, small, dark tumors about the nasal orifices, the end of the tail becomes knobby, and bean-like excrescences are common on the edges of the eyelids; these always in association with an intense conjunctivitis. These tumors, which commonly show superficial ulcerations, contain great numbers of spirochetes. Ulcerated papular syphilides may occur around the anus and vagina. In some instances the inoculation of extracts of various of the internal organs of such animals, into normal dogs, induced lues in the latter. Luetic testicles or the occurrence of eye manifestations seem to offer no protection

against further inoculations, nor do the sera of dogs, repeatedly injected with spirochetes, protect other dogs from the disease; such sera are likewise of no therapeutic value. Uhlenhuth and Mulzer were unable to cultivate the *spirocheta pallidum* from infected animals. With reference to transmission of the disease, it was found after intravenous injections of the spirochete, the organisms were able to penetrate the sound placenta within five minutes and could be demonstrated in the fetus. The injection of blood from individuals in the primary or secondary stage of lues, caused a specific orchitis in 78 per cent. of the cases; even the blood of persons having latent syphilis and showing a negative Wassermann reaction can be infectious. Uhlenhuth and Mulzer conclude therefore that lues is essentially a chronic septicemia.

Theory of the Wassermann Reaction.—PRAUSNITZ and STEM (*Zentralbl. f. Bakteriol.*, 1913, lxi, 545) in going over the subject of the Wassermann reaction it was found that both aqueous and alcoholic extracts of luetic livers gave complete complement fixation in the presence of luetic sera; alcoholic extracts were much more potent and reliable; alcoholic extracts of the residue from the syphilitic livers were inactive. It was found that intravenous injections, into dogs, of either of the above potent extracts would induce a positive Wassermann reaction in their sera; controls, with normal extracts were always negative. Since experimentally the production of an active antibody results from the introduction of a substance or substances soluble in alcohol, and probably of a lipid nature, while on the other hand only proteids induce antigen production, it seems reasonably certain that the Wassermann reaction is not a true antigen-antibody process. The reaction is to be considered characteristic when positive, but not specific. Whether the lipoids in the reaction originate from the luetic tissue or from the spirochetes, remains to be seen.

The Blood Picture in Status Lymphaticus.—SIESS and STOERK (*Wien. med. Woch.*, 1913, lxi, 1123) give a report of 23 cases, diagnosed by reason of the following symptomatology: (1) Atypical arrangement of the hair; (2) abnormal length of the extremities; (3) scaphoid scapulæ; (4) a wide pelvis in males, narrow in women; (5) adiposity of the reverse type, in the lower half of the body in males, upper half in females; (6) poor development of the breasts; (7) general glandular hyperplasia; (8) small but elongated heart associated with a strong apex beat and an accentuated aortic second sound; (9) low blood-pressure; (10) psychoneurotic manifestations; (11) vagotonia; (12) infantile type of epiglottitis. The blood findings in such cases showed few deviations from the normal picture. Thus the red-blood corpuscles varied between 3,000,000 to 5,000,000, the hemoglobin being generally high. Contrary to a general belief the white cells are not consistently low-ranging in this series from 4300 to 10,000. As regards the various white cells, the neutrophilic leukocytes, large mononuclears, and transitionals are within normal limits; lymphocytes rarely exceed 2000 per c.c. but quite characteristic of them is their unusually abundant protoplasm. Eosinophiles are consistently low, whereas the abundance of blood platelets is a noteworthy feature. Functional tests of the activity of the bone-marrow, made by means of gelatin infections,

showed an increase in neutrophilic leukocytes considerably lower than normal; on the other hand the mononuclear elements not only failed to show the customary decrease, but in 4 cases were absolutely increased.

SURGERY

UNDER THE CHARGE OF

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OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND
ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Traumatic Epilepsy and its Surgical Treatment.—MATTHIAE (*Deut. Zeitschr. f. Chir.*, 1913, cxiii, 417) collected from the literature and studied 326 cases of traumatic epilepsy, which had been operated on. Of these 60 were of the general and 266 of the Jacksonian type. Favorable results (cure with permanent recovery or recovery lasting some years) were obtained in 96 cases, of which 81 were of the Jacksonian and 15 of the general type. The results were unfavorable (no influence, made worse, or death) in 81 cases, of which 59 were of the Jacksonian type and 22 general. The remaining cases were observed for too short a time or either the results or the time of observation were not given. The time of observation after which one can speak of a permanent cure, should be at least five years. In these 326 cases there were only 4 in which the attacks recurred after they had ceased for several years. In one they recurred after a cure of four years, in two others after five years and in the fourth after six years. The time of observation should be, therefore, at least five years. In all, 24 cases were followed for more than five years, of which 21 were of the Jacksonian and 3 of the general type. A cure (for under five years but one year at least) was obtained in 40 cases (Jacksonian 36, general 4). Improvement was obtained in 27 (Jacksonian 19, general 8). There was no improvement in 59 cases (Jacksonian 42, general 17). The condition was made worse, evidently from the operation itself, in 3 cases, and 19 died as the result of the operation (Jacksonian 16, general 3). Death was due to shock or collapse in 6 cases, meningitis in 5 cases, status epilepticus in 3 cases (one of which died as the result of tonic contraction of the diaphragm). In one case death was due to pleuropneumonia and secondary hemorrhage. The favorable cases were all observed at least one year, while in the failures the period of observation was sometimes less. According to experience up to the present time, improvement and cure may develop only a long time after operation, just as the improvement after operation may disappear again after a time.

The Operative Treatment of Prostatic Hypertrophy.—ENGELMANN (*Deut. Zeitsch. f. Chir.*, 1913, cxxiv, 116) discusses the treatment of prostatic hypertrophy by vasectomy, a suprapubic fistula of the bladder, the galvanocaustic incision of Bottini, and prostatectomy. The latter has become the operation of choice, especially the suprapubic prostatectomy. In discussing vasectomy, he says that when the gland is soft and not very large, this operation produces a diminution in the size of the gland and in the retention of urine and subjective symptoms. He employed it in about 100 cases, and obtained satisfactory results in over 50 per cent. He regards it as suitable (1) for the early stages of the affection when there is transitory but frequently repeated complete retention of urine, hemorrhage and subjective symptoms; (2) as a preliminary operation to prostatectomy or the Bottini operation in patients inclined to epididymitis; (3) when the condition of the patient forbids a severe operation. In the last group of cases, if catheterization is too difficult or impossible, he sometimes makes a suprapubic fistula in the bladder, when vasectomy fails. In the last eight years he has done 91 Bottini operations and 31 suprapubic prostatectomies. The indication for operation is always retention of urine, complete or incomplete, persisting in spite of catheterization, sounds or vasectomy. Most of his cases had cystitis, some had pyelitis or pyelonephritis, which do not contra-indicate the operation but do affect the choice of operation. The Bottini operation should not be done in patients with pyelonephritis. At first this operation was done under local anesthesia, but later lumbar anesthesia was found to be more effective. Three incisions in the gland by the galvanocaustic incisor, were employed in almost all cases. In rare cases, especially when the prostate was large, four were made. Of 90 cases thus treated 69 were cured, 10 considerably improved, 3 not improved, and 8 died. In other words, 87.8 per cent. gave good results and 12.2 per cent. were failures. Of the 90 cases, 75 suffered from cystitis and 23 from pyelitis or pyelonephritis. Of the 8 who died from the operation, 7 had chronic pyelonephritis, exacerbations of which with the associated urosepsis were responsible for 6 of the deaths. In these 31 prostatectomies, he had 6 deaths. The indications for the choice between the two operations are as follows: Prostatectomy is to be preferred when the prostate is very large and when a pedunculated middle lobe projects into the bladder. With a relatively small hypertrophy, especially if an hypertrophied middle lobe is in the form of a barrier to micturition, the Bottini operation is to be preferred. It is to be done when the prostate is very large, only when the general condition contra-indicates a prostatectomy. When there is infection of the urinary tract especially a pyelonephritis, prostatectomy gives better drainage. If the kidney function is much impaired, palliative treatment (cystostomy, vasectomy) is to be employed

The Pathogenesis of Hydrocele.—ZESAS (*Zentralbl. f. Chir.*, 1913, xl, 1291) says that it is already known that hydrocele is much more frequent in the warm and tropical climates than in the cold. Some writers ascribe this to a more active function of the testicle in warm countries, while others ascribe it to the direct effect of the warmth. According to the latter view the warmth produces a relaxation of the

scrotum and spermatic cord, because of which the testicle and its enveloping structures are exposed to mechanical irritation. The following case serves as an illustration of this method of origin: A young farmer was affected at every harvest time by a one-sided hydrocele, which disappeared completely in the autumn. He was advised as a prophylactic measure to wear a suspensory bandage during hard work in the warm season. This was followed by complete relief from the hydrocele. Much more frequently the hydrocele is due to infections occurring in the warm climates, particularly to malaria. In many cases operated on by Zesas, the patient had suffered or was still suffering from malaria. It was observed also that in those patients who still suffered from malaria together with the hydrocele, there were inflammatory changes in the testicle and epididymis, while in those patients who had recovered from their malaria, the testicle appeared to be normal and the hydrocele was the result of the preceding inflammatory process. Inflammations of the testicle are not very rare in malaria. During the febrile attacks swelling of the testicles and epididymes is the rule, and it is usual for the disease to be associated with a serous vaginitis. As a rule these symptoms disappear completely from rest in bed and the administration of quinine. Occasionally atrophy of the testicle or thickening of the epididymis remain. The hydrocele appears to be a secondary manifestation of malaria and is either an accompanying symptom of malarial orchitis or epididymitis, or is the remains of such a process. Recurrence of the hydrocele after a radical operation, says Zesas, cannot be excluded with the existence of the anatomical changes in the testicle.

The X-rays in Gouty Arthritis.—JACOBSON (Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1913, xxvi, 531) says that joint diseases due to a gouty diathesis are not always diagnosed from the non-gouty cases by the clinical manifestations. The so-called chronic rheumatism (atrophic arthritis) often shows the same clinical picture. Laboratory methods are often not available. The x-rays are not without value and deserve a place among the other diagnostic methods. In estimating the value of the x-ray examinations of gouty joints and how far they can aid in the differential diagnosis between this and other joint diseases, Jacobson says: Even when the diagnosis of gout is established, one or several skiagraphs should be made because they show the grade of changes in the joint by the disease. For the prognosis it is important to know whether only simple changes (bone atrophy, narrowing of the joint space) is present or the whole joint destroyed. He disagrees with Gélibert and Lumière who advise that the tophi should be removed, because by so doing one could not prevent the irregular bone changes which would later interfere with the function of the joint, and limb. Gouty arthritis can give, by the x-rays, signs which are peculiar to it and which, therefore, may be regarded as pathognomonic. These are the changes in the bones, which consist particularly in the deposits in the bone showing in the x-ray plate as transparent defects in the bone. They may be round, oval or irregular, but are present, however, in only a small percentage of the cases in which the clinical picture is only that of a chronic rheumatic arthritis (arthritis atrophicans), although they are then of much diagnostic importance.

THERAPEUTICS

UNDER THE CHARGE OF

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Splenectomy in Treatment of Pernicious Anemia.—HIRSCHFELD and KLEMPERER (*Therapie d. Gegenwart*, 1913, liv, 385) report two cases of pernicious anemia in which marked improvement followed splenectomy. They were led to try this radical procedure by the fact that a previous patient with Banti's disease developed a pronounced polycythemia a year and a half after a splenectomy had been performed. In this patient the hemoglobin rose to over 120 per cent. and the number of red blood cells increased to seven and eight million, and the blood picture was in marked contrast to the former severe secondary anemia. In addition there are also a number of other cases on record in which a polycythemia has developed after a splenectomy for rupture of the spleen. They believe that probably pernicious anemias of recent origin will be more favorably influenced by splenectomy than cases of long standing. The most striking effect observed in the two cases reported by Hirschfeld and Klempcrer was the marked and prompt increase of nucleated red blood cells in the blood. The effect produced was so striking that it showed conclusively, according to Hirschfeld and Klempcrer, that the splenectomy stimulated the production of red blood cells on the part of the bone marrow. In one patient the hemoglobin rose from 30 to 55 per cent. in one month and to 80 per cent. after two months, with a corresponding increase in the number of red blood cells. Although the blood of these patients still has certain features of pernicious anemia, especially the presence of numerous megalocytes, yet the results obtained justify the conclusion that this procedure has a definite influence in stimulating the production of red cells.

The Effect of Atophan and Novatophan on the Endogenous Uric Acid Excretion of Normal Men.—HASKINS (*Jour. of Pharm. and Exper. Therapeutics*, 1913, v, 63) investigated the effect of atophan and novatophan upon the endogenous uric acid excretion in 21 normal men. All of them had been on a purin-free diet for one week before atophan or novatophan was administered. The first 16 reported in the table showed over 200 mg. increase of uric acid excreted under the influence of the drug. This increase was most marked on the day following the administration of the drug. Four others showed a less marked increase, but in 1 case the increase was not apparent until the second day. The one subject that showed no increase of uric acid was only examined on the day following the administration of the drug and Haskins suggests as an explanation that in his case the elimination might have been delayed. Judging by the results

obtained by Haskins, atophan seemed to be more efficient in its action than novatophan. Investigation, undertaken to compare the excretion of the period after taking the drug with the period before taking it, showed that the excretion of uric acid was at a distinctly lower level in the period after the administration of the drug than preceding it. Haskins believes that the results of his investigations point strongly to the possibility that the main effect of atophan and novatophan is to drain uric acid out of the blood, leaving the uric acid content of the latter subnormal.

Artificial Pneumothorax in the Treatment of Chronic Infection of the Pleura and the Lungs.—FLOYD (*Boston Med. and Surg. Jour.*, 1913, clxix, 713) reported two years ago with Robinson a series of 28 cases of pulmonary tuberculosis treated by artificial pneumothorax. Of this number 8 cases had either shown an entire arrest of an active process or were approaching that condition. The remaining 20 cases had secured relief of symptoms to a greater or less degree. Of the arrested cases, six are in excellent condition at the present time. One has died, through no fault, however, of the method and one has, within the last year, shown an extension of the old process into the previously collapsed portion of the lung. Floyd says that during the past four years he has treated a large number of cases of pulmonary tuberculosis by this method. Some of these have been under treatment primarily for the relief of one or more symptoms, such as persistent cough, or hemoptysis. In the great majority, however, the object of the treatment has been to arrest an advanced active process. In the larger number of cases reduction in temperature, relief of cough, diminution of expectoration and an increase of body weight have occurred. In several cases where the character of the disease was that of a chronic toxemia with an advanced pulmonary lesion, the results of the compression of a portion of the active lung has markedly diminished toxic absorption. Improvement in circulation, gain in weight, and increase of strength followed, even where the extent of pneumothorax was limited. In one case of pyothorax secondary to an advanced tuberculous process of the lung in which the pus was withdrawn and the fluid replaced by nitrogen no results were obtained on account of the dense unyielding condition of the consolidated lung. In cases of pulmonary tuberculosis complicated with a secondary infection results have been fairly good only where collapse of the lung has been extensive. The compression of a portion of the lung tends merely to diminish the amount of sputum and reduce temperature. The action of pyogenic organisms is not checked and lung destruction slowly advances. In the unilateral cases of active tuberculosis not only relief of symptoms but arrest of the disease has been obtained. The time required to accomplish this has varied with the extent and activity of the disease. The tendency in most instances is to lengthen the interval of injections too rapidly and even stop them altogether before permanent arrest is assured. With artificial pneumothorax as with other methods of treatment of tuberculosis relapses occur and a renewal of the treatment may be necessary. Floyd says that his experience with the use of artificial pneumothorax has shown him that only a relatively small

number of cases are really suitable for this treatment. Well marked or advanced strictly unilateral cases are not common even in large clinics for pulmonary tuberculosis, and some observers believe that such cases are always bilateral. If this type of case is strictly adhered to the results obtained will be uniformly good and the percentage of patients markedly improved or arrested will be as large as 40 per cent. or 50 per cent. If, on the other hand, almost any otherwise hopeless case in which satisfactory compression can be obtained, is given a chance of obtaining relief at least from persistent symptoms, the results will not be brilliant. Artificial pneumothorax will be of real aid in the chronically recurring tuberculous pleural effusions, and in some cases of bronchiectasis and pulmonary abscess in which the inflammatory conditions are not too extensive. But even if this group of diseases may be benefited by the use of this method its field in the treatment of diseases of the chest will still be relatively a narrow one. It is most applicable where the patient is under the supervision of hospital or sanitarium management and has failed to do well with the older and well-established methods.

An Experimental Study of the Antiseptic Value in the Urine of the Internal Use of Hexamethylenamin.—HINMAN (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1601) in his conclusions states that the conversion of hexamethylenamin into formaldehyde is a simple chemical process which will readily occur in an acid medium but will not occur in an alkaline medium. The amount of excretion of hexamethylenamin in the urine is influenced by the size of the dose, by the frequency of administration and by the character of the changes that occur in the acid contents of the stomach. The amount of the subsequent conversion of this hexamethylenamin in the urine is dependent on the degree of urinary acidity, on the duration of exposure to the influence of this acidity and on the percentage concentration of the drug in it; and in order to give formaldehyde conversion in antiseptic amounts the urinary acidity should be greater than 2 c.c. of tenth-normal sodium hydroxide for 10 c.c. of urine. A low acidity may be temporarily increased by feeding certain acid-producing drugs, and this increase in acidity may often be maintained by giving these drugs alternately. Disease of the kidney has no influence whatsoever on the formaldehyde content of the urine. At the level of the kidneys hexamethylenamin in doses of 15 grains three times a day has no antiseptic value. Formaldehyde is present in the bladder urine in some amount in practically every case receiving 15 grains of hexamethylenamin by mouth three times a day, but this dosage is too small a routine from which to expect a reasonable antiseptic benefit in every case. The allied hexamethylenamin compounds do not give greater antiseptic values than pure hexamethylenamin. Hexamethylenamin is dispensed under many proprietary names, such as urotropin, formin, aminoform, cystogen, etc. Certain of these are less irritant, but none of them liberate more formaldehyde than the pure drug, and in most cases not so much. In addition to these there are a number of other proprietary preparations for which an action superior to hexamethylenamin is claimed but of four of these, helmitol, hexal, saliformin and myrmalyde, studied by Hinman, none gave as good a formaldehyde content as hexamethylenamin.

Intravenous Injections of Neosalvarsan with Syringe.—ZUMBURCH (*Wien. klin. Woch.*, 1913, xxvi, 1305) has given 337 intravenous injections of neosalvarsan in concentrated form by means of a syringe to 149 cases and considers that this method is far preferable to the gravity method of injecting dilute solutions of neosalvarsan. The chief advantages are the rapidity of treatment and the simplicity of the apparatus. The usual dose of 0.75 to 0.9 gm. of neosalvarsan is dissolved in 20 c.c. of solution and the injection is made by means of a 20 c.c. Ricord syringe. The only apparatus required consists of the syringe, needle, and sterile glass for making the solution.

The Intravenous Injection of Neosalvarsan in Concentrated Solution.—SCHRIBER (*Münch. med. Woch.*, 1913, lx, 1993) advocates the use of intravenous injections of a concentrated solution of neosalvarsan in place of the injection of the more dilute solution, usually given. The usual dose of 0.75 gm. of neosalvarsan dissolved in 10 c.c. of normal salt solution is injected directly into the vein by their method. Schriber has used these injections extensively and has given them to individual patients once a week over long periods of time without untoward effects. These injections give rise to no greater general reaction than those observed when the drug is given in more dilute solutions. No irritation at the site of injection has been observed with the use of this concentrated solution. Schriber is of the opinion that this method of injection is a distinct advance and makes neosalvarsan a practical drug for general practice.

Radium in Internal Medicine.—ROWNTREE and BAETJER (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1438) give a summary of the physiological and therapeutic effects of radium as observed by many European authors. They find that the consensus of opinion is that the use of radium is attended with an increased urinary uric acid output and that disappearance of deposits (tophi or artificial deposits) is hastened. Radium is given in the form of baths in radio-active water and the benefits derived in many of the European spas is now attributed to the inhalation of radium emanation as it constantly escapes from the surface of the water. Radium is also given by subcutaneous injection, as a local application such as compresses to the skin and internally by drinking radio-active water. The best method is by inhalation, but this is very expensive requiring a special air tight room or cabinet. The authors believe that the value of radium is unquestionably established in chronic and subacute arthritis of all kinds (luetetic and tuberculous excepted), acute and chronic joint and muscular rheumatism, in gout, sciatica, neuralgia, polyneuritis, lumbago, and the lancinating pain of tabes. In certain other diseases it is said to be of value, but here the evidence is not so convincing. This list is a varied one and includes chronic bronchitis, chronic pharyngitis, pneumonia, myocarditis, arteriosclerosis, vasomotor disturbances, Raynaud's disease, scleroderma, idiopathic enlargement of the lymph nodes and chronic constipation. Rowntree and Baetjer give tables to show the results obtained in the different diseases of 471 cases of chronic arthritis and chronic rheumatism as described by 23 authors, 371 were improved, and of these 102 were cured. Of 24 cases of arthritis deformans reported

by seven observers, 16 showed improvement. Of 59 cases of muscular rheumatism, 49 were either cured or improved. Of 166 cases of gout, 86 were influenced for the better. Of 59 cases of neuralgia, 47 were improved, of which 25 were practically cured. Of 115 cases of sciatica treated by 18 different authors, benefit was observed in 91 instances, although some of the cases were of long standing. In 44 cases of tabes, the lightning pains were alleviated in 26 instances, for long periods of time in some instances. Rowntree and Baetjer also cite a series of 18 cases including a considerable variety of affections where their personal experiences with this method of treatment were not so favorable, as the published work of European observers indicates. However, they do not wish to draw conclusions from so small a series and furthermore the cases treated have been a severe test of the treatment since they comprised these cases which had been given the benefit of all other forms of treatment without bony improvement. Rowntree and Baetjer believe that the introduction of radium emanatoriums in a large number of German spas, as well as the establishment of a radium institute in Berlin express confidence in this method on the part of the profession abroad and this subject should be carefully investigated until its real value can be definitely established and its limitations rationally outlined.

PEDIATRICS

UNDER THE CHARGE OF

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Treatment of Diphtheria Carriers with Bouillon Cultures of Staphylococcus Pyogenes Aureus.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1913, x, 298) reviewed the reported cases of diphtheria carriers treated by cultures of the staphylococcus pyogenes aureus and found the total number reported to be about 50, and with a few exceptions the observations were confined to the United States. In almost all the cases, the throats of the carriers were sprayed or swabbed with a bouillon culture of the staphylococcus. In most of the cases negative cultures were obtained in 48 to 72 hours after this form of treatment had been begun. The method was shown to be most successful in typical carrier cases and less so in cases with clinical symptoms. Rolleston used this treatment in 10 cases, comprising 4 adults, and six children. In 8 the fauces and in 2 the nose alone had been involved and all had reached an advanced stage of convalescence. The palate, fauces, and in the nasal cases the nostrils as well were sprayed 3 or 4 times a day with broth cultures of pure staphylococci incubated for 18 to 24 hours. In all but 2 cases a mild form of sore throat was produced with considerable malaise but with very slight fever. These symptoms were of short duration and were not followed by any complication. The average time the treatment was begun in this series was the fifty-second day of the condition. In the 6 faucial cases the findings became

negative within two to seven days after starting treatment. In the 2 nasal cases it was ineffective. This method should not be employed except in the late stage of convalescence and it is best to confine it to chronic carriers. It offers the best form of treatment but entails some degree of discomfort. Among the previous investigators no complications were noted except Lorenz and Ravenel who mention coryza, very mild laryngitis, and nasal furuncles occurring among their cases.

Acute Acid Intoxication in Children.—THOMAS C. McLEAVE (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1764) reviews the theories of production of acid intoxication and gives the symptoms and treatment. This condition may occur in children aged from eight months to ten years. It may usher in an acute infectious disease or the attacks may be recurrent. Some chronic focus of infection is probably always present, such as an inflamed appendix or more commonly diseased tonsils or adenoids. The toxins from whatever source cause a condition in the liver function which produces faulty metabolism of carbohydrates and especially of fats and proteins. As a result, toxic bodies such as acetone and diacetic acid appear in large quantities in the urine and acetone is markedly noticeable on the breath. The nervous element is undoubtedly a factor in producing the condition, and a catarrhal condition of the nasopharynx is usually present. Characteristic symptoms are anorexia, coated tongue, a bluish pallid ring around the mouth and eyes with flushing of the cheeks, coryza with variable cough, pallor, sunken eyes, dry and cracked lips, foul breath with odor of acetone, vomiting of large amounts of fluid, rapid emaciation, scanty urine, constipation, and moderate fever. The duration of the attack is from two to seven days but deaths from this cause are very rare. The treatment consists of eliminating any possible focus of infection, a dietary low in fats with ample amounts of carbohydrate. Citrus, fruit juices, and grape-juices are also valuable. Fatigue and undue excitement should be avoided. Sodium bicarbonate in one to two dram doses weekly, and periodic emptying of the large bowel tend to abort the attacks. During the attack sodium bicarbonate can be given in 60-grain doses every three or four hours by mouth or rectum. Sugar must be given, preferably dextrose, in 4 per cent. solution with alkali, either by mouth or rectum. Both the sodium bicarbonate and the dextrose can be given in solution intravenously if the case is urgent. Saline infusions are given for the drying-out of the tissues, and opium, chloral, and the bromides control the nervous manifestations.

Some Unusual Phases of Child Hygiene.—MARY SUTTON MACY (*Archiv f. Pediatrics*, 1913, xxx, 848) points out the importance of protecting the child (from infancy to adolescence) from the ill effects of psychic trauma, which are not by any means all sexual. The epidemic of Freudism in this country threatens to restrict the term "psychic trauma" in its meaning to the sexual character. Macy mentions a large number of cases in children from ten to eighteen years initiated by a psychic trauma, which closely simulated a beginning Basedow's disease. In none of these cases has the initial shock been in any way sexual. She also mentions 30 cases of chorca having a history of psychic trauma, in no way sexual, as the point of origin

for the neurotic symptoms. She calls attention to contributory effects of nervous shock in initiating both of these nervous conditions. She defines psychic trauma as a term embracing all nervous shocks which arrest or retard mental processes, and includes under the term acute shock from fright, anger, grief, joy, fear, etc., and chronic shock from repeated disappointment and mental fatigue from uncorrected defects of vision, hearing, etc. In public schools a crowded curriculum and forcing children forward at a fast rate is a detriment to health and tends to produce mental and physical inadequacy. Both diseases mentioned above are aggravated, if not more or less indirectly caused by psychic trauma. Therefore, all obvious causes of nervous strain within control of public school authorities should be prevented. The majority of those in immediate charge of our schools are absolutely unintelligent on this vital subject of caring for the health of the child. Medical school inspection has done practically nothing to control and prevent disability from over-pressure, crowded curriculum, and nervous strain during puberty and early adolescence.

OBSTETRICS

UNDER THE CHARGE OF

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Imidazolylathylamin in Obstetric Practice.—JAEGER (*Zentralbl. f. Gynäk.*, 1913, viii) reports the results of this agent in obstetric practice. It is a preparation derived from ergot and from histidin by the action of nitric acid. It is supposed to stimulate unstriated muscular fibers. It acts upon the muscular fibers of the uterus, the muscular tissue in the bronchial tubes, the iris, and the bladder. It probably has some action upon the unstriated muscle of the bowel, the arterioles, and the spleen. It does not seem to affect the heart directly. On blood pressure, it produces a differing action in different animals. In some, the blood pressure rises; and, in others, sinks. The action of the salivary glands and pancreas is increased by the hypodermic injection of this substance, while the secretion of urine is not influenced. This agent was tried in the case of a puerperal woman, in doses of 30 drops of a solution 1 to 1000, given three times daily. This agreed with the patient, and produced no disagreeable effects. It was compared with other preparations of ergot. Involution seemed to proceed more efficiently, and the after-pains were less frequent, and shorter. It was used to increase the vigor of uterine contractions in 25 cases, 13 primiparæ and 12 multiparæ. It was given by intramuscular injection in the gluteal region, or subcutaneously in the arm or upper portion of the thigh. These injections were not painful, but produced redness at the point where the needle entered. Varying doses were

tried, and the effect noticed upon the mother and the child as well. No influence could be detected upon the fetus, but in some of the mothers the head and face were flushed, the heart acted more vigorously, there was erythema, flatulence, and vomiting. In the experience of Jaeger, small doses produced the best results, and on the whole, the remedy seemed quite as efficient, and in many respects better than the usually employed preparations of ergot.

The Complications and Variations of Eclampsia.—HALLIDAY CROOM (*British Med. Jour.*, December 21, 1912) calls attention to what he terms *pseudo-eclampsia*. His patient was a woman seven months, in her second pregnancy, who had severe fits for two days, with marked coma. The urine was normal; there was no evidence in the eyes or limbs of any lesions of the nervous system. The patient died, and at autopsy a cholesteatoma the size of an orange was found in the brain near the anterior end of the left cerebral hemisphere opposite the superior middle and inferior frontal convolutions. In another case in which eclampsia was suspected, at autopsy meningitis was found to be the cause of the convulsions. In discussion, Fordyce described two cases treated as eclampsia in which at autopsy cerebral hemorrhage was found. The etiology of eclampsia was the subject of discussion in a joint meeting of the sections of Pathology and Obstetrics of the British Medical Association, (*British Med. Jour.*, October 26, 1912). Ballantyne believed that eclampsia was the result of pregnancy with renal and hepatic inadequacy, and possibly external and internal disturbances, which increased the strain upon the kidneys and nervous system. Unquestionably, toxemia causes eclampsia. Primary toxemia may result from disturbances in the mutual metabolism of mother and fetus, while the secondary toxemia which develops and causes the convulsions must be left to changes in the kidneys, liver, and other glands. The successful treatment addressed to toxemia supports its claim to be the cause of eclampsia. In his personal experience, his results improved greatly in proportion as he treated eclampsia for the toxemic condition present, his maternal mortality under this treatment being 9.6 per cent. Teacher reviews the literature of the subject, and describes the changes found in the kidneys and suprarenals in 21 cases. Smyly reviews the literature of the subject, and considers that Stroganoff's statistics indicate successful treatment. Kerr used medicinal treatment in cases where the cervix was obliterated and there were indications that labor was about to take place. If the birth canal is undilated, he would deliver by section.

HEINRICHS DORFF (*Zentralbl. f. Gynäk.*, 1912, iv) reports the case of a primipara who died half an hour after delivery with forceps, after moderate hemorrhage, and apparently from failure in the action of the heart. At autopsy, the liver was found enlarged, with extravasations of blood under the capsule and staining in various portions of the gland. The interesting feature of the case was the absence of convulsions, there being present hemorrhage and extensive lesions in the liver characteristic of eclampsia.

LADINSKI (*Amer. Jour. Obstet.*, July, 1912) reports eclampsia complicated by the birth of a monster, consisting of two fetal bodies joined together through the trunk and with one head.

BAUREISEN (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft $\frac{1}{2}$) raises the question whether eclampsia is a reaction of immunity. He believes that placental tissue exercises the function of an antigen, and that disturbances of the nervous system in the first months of pregnancy, and in the digestive organs, are the results of the development of immunity through the absorption of placental products.

DIENST (*Archiv f. Gynäk.*, 1912, Band xevi, Heft 1) has made experiments to determine the influence of fibrin ferments in the causation of eclampsia. He believes that pregnancy predisposes to derangements of the circulation, and that fibrin ferment is readily produced in excess. This may become a toxic product, and readily bring about degenerative changes seen in those organs most closely concerned in the process of metabolism.

Hematomyelia complicating eclampsia is reported by LEBICH (*Zentralbl. f. Gynäk.*, 1912, xxxivii). The patient was a primipara at term, in labor, and having severe eclamptic convulsions. Between the first and second the temperature rose to between 105° to 106° F.; the pulse was small and feeble. The patient complained of intense pain in the neck and right shoulder. The cervix was partly dilated and the head in the pelvic cavity. Delivery was effected by incising the cervix and using forceps. The child was living. After delivery, the blood pressure was 108, and the urine contained 12 per cent. albumin. There were no more convulsions, and the patient gradually recovered. She developed nervous symptoms of paralysis in some of the muscles, spastic in nature, and her final recovery was complicated by paresis in several groups of muscles.

Pseudo-eclampsia is the subject of a paper by POLANO (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxx, Heft 2). He reports 2 fatal cases, with autopsy, one of whom had epileptic convulsions with albumin in the urine, and was delivered by incising the cervix and applying forceps. On autopsy there were extensive degenerative changes in the glandular organs and beginning hypostatic pneumonia. The second case was brought to hospital unconscious, the urine showing casts and albumin. The cervix was tightly closed, and the urine brownish-red in color. The patient was delivered by section, and, upon autopsy the characteristic changes in eclampsia were found in the various organs.

PERSSON (*Archiv f. Gynäk.*, 1912, Band xeviii, Heft 1) draws attention to the relation between eclampsia and puerperal paresis. While they are distinct conditions, their common element is the presence of fetal material in the blood of the mother. He believes that this material produces the characteristic alterations in the blood, and thinks he has had good results from the administration of potassium iodide. He believes that it produces this effect because it lessens the amount of saline material in the blood.

ESCH (*Archiv f. Gynäk.*, 1912, Band xeviii, Heft 1) takes up the familiar question of the toxicity of the urine in eclampsia. He believes in pregnancy that the toxicity of the urine is not much increased, while it is lessened during labor, increasing somewhat the fourth and fifth day of the puerperal period. From experiments upon animals he found that intraeranal injections of urine from healthy, non-pregnant patients, from those with carcinoma of the uterus, from

those in labor and in the puerperal period, and from women having eclampsia, produces in guinea-pigs light or severe anaphylactic shocks; and this was confirmed by autopsy. Subcutaneous or intraperitoneal injections of urine from patients not evidently toxic, produced no symptoms in white mice. Where decomposed urine, or altered urine was employed, death followed with hyperemia of the abdominal organs. The toxicity of urine measured by the temperature reaction was very little increased in healthy pregnant patients. In patients in labor, it was somewhat lessened, and in puerperal patients, somewhat increased. In 2 cases of severe eclampsia occurring during labor, the urine taken in the period of dilatation was exceedingly toxic, while in the third case there were slight convulsions, and the urine was scarcely altered from the normal.

A curious contribution to the therapeutics of eclampsia is made by WALCHER, JR. (*Zentralbl. f. Gynäk.*, 1912, xlii). Acting upon Sellheim's suggestion that the breasts contain toxins which have a part in the production of eclampsia, he has treated, in the clinic at Stuttgart, 11 cases of eclampsia by extracting colostrum from the breasts in many cases, followed by the infiltration of salt solution. The results seem to indicate that this procedure may be useful in checking convulsions.

ZINSSER (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxx, Heft 1) has investigated the function of the kidneys in eclampsia. He believes that in eclampsia the chlorides are retained and not excreted normally by the kidneys, and that this has to do with the production of eclampsia. He has made observations to determine the percentage of sodium chloride in the blood of eclamptics, and also in the excretion of eclamptics at the time of the convulsions. His cases numbered 31, and for 14 he gives curves illustrating his observations. He finds that in eclamptic cases with dropsy, where there is a sudden and permanent arrest in the excretion of chlorides, usually in the form of chloride of sodium, and where there is no other clinical reason for this phenomenon, that this constitutes a symptom of dangerous and often fatal intoxication. When, on the other hand, the percentage of chlorides in the urine is high, it is a symptom which justifies a favorable prognosis.

GYNECOLOGY

UNDER THE CHARGE OF

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Prophylaxis of Carcinoma of the Cervix.—BOSSI (*Zentralbl. f. Gyn.*, 1913, xxxvii, 1000) has recently issued an appeal to all gynecologists to consider more carefully what he considers the true prophylaxis of cervical cancer, namely, the early, *surgical* treatment of all minor, non-malignant injuries and inflammations of the cervix. To treat

such conditions with local applications, caustics, etc., as is so commonly practiced, is, in his opinion, utterly unjustifiable; the chronic inflammations and tissue hyperplasias that are caused by such treatment are, he thinks, often the direct cause of a subsequent malignant development. All ulcers of the cervix should be removed, hyperplastic areas of endometrium curetted away, and small lacerations repaired by suitable plastic operations; if this policy were uniformly carried out we would see vastly less uterine cancer than is now the case. Bossi says that as he looks back on his years of practice he finds that he has performed such plastic operations on over 7000 patients, and so far as he has been able to determine, in no single instance has one of these women subsequently developed a cervical carcinoma. A record such as this, together with the fact that cancer is in no wise contagious, is for him proof positive that the disease is absolutely non-microbial, but purely histologic in origin; he thinks that a truly humanitarian and scientific undertaking would be a propaganda against uterine cancer which should have for its basis the early, reparative, surgical treatment of benign affections of the cervix and uterine cavity.

Hydrotherapy in Gynecology.—In a communication presented before the Congress of Physicians and Naturalists, held in Vienna last September, KLEIN (*Frauenärzt*, 1913, xxviii, 541) reports on the results obtained in the treatment of various gynecological conditions by means of hydrotherapy in the year and a half since the plant was installed in the Wertheim Clinic. He says that the results were in general exceedingly good, and in some instances most astonishing. The indications for this form of therapy include both functional and organic disturbances; especially good results were obtained in the treatment of all the types of disease commonly grouped under the term "sexual neurasthenia," but many true organic conditions also show marked improvement or complete cure. Among these may be mentioned particularly perimetrial adhesions, exudates following salpingo-oophorectomy, extensive parametrial exudates, chronic inflammatory adnexal masses, etc. In conjunction with various forms of hydrotherapy, mud baths have also been found of great benefit in some of these chronic inflammatory lesions. Klein emphasizes the importance of a thorough mastery of the technique of this form of therapy in all its details, and thinks that much of the skepticism which exists toward it is the result of poor results obtained from a lack of knowledge as to the indications and contra-indications on the one hand, and of the technique on the other.

Formalin Treatment of Leukorrhea.—The technique and results of a new form of treatment for leukorrhea, recently introduced at the Baudeloque Clinic, are described by LE MASSON and MARCHAL (*Ann. de Gyn. et d'Obst.*, 1913, xl, 731). This consists in the introduction into the vagina of nascent formalin gas, a process which may be accomplished by one of several methods. The simplest is merely to fold a few crystals of potassium permanganate in a small square of gauze, sprinkle it well with full strength formalin solution, and introduce it by means of dressing forceps into the vagina through a speculum.

More thorough and satisfactory application may be secured, however, by the use of some form of vaporizing apparatus, while for use by the patient herself, a special appliance, known as the "formojecteur" has been devised. This consists of an egg-shaped receptacle, which may be taken apart in the middle, and which contains a separate compartment for water, the whole being connected with a short tube and douche nozzle. To use it, the egg-like receptacle is opened, and 1 gm. of crystalized potassium permanganate placed in the bottom. It is then closed again, and the water compartment filled with 1 c.c. of a mixture of equal parts of commercial formalin and water. The patient then introduces the douche nozzle into the vagina in the ordinary manner, and by pressing with her thumb on a small piston which communicates with the chamber containing the formalin solution, forces this into the main receptacle containing the permanganate, with the resulting generation of formalin gas. This, of course, passes off through the nozzle into the vagina. Le Masson and Marchal have found formalin gas, applied in this way, to have a marked drying action on leukorrheal discharges, transforming profuse mucopurulent discharges into a thin, watery type, which in turn soon completely disappears. This dessicating action is followed by a certain amount of tissue retraction, resulting in cicatrization of mild degrees of cervical endometritis, and diminution of erosions about the external os. To be thoroughly efficacious, however, the treatment should be kept up faithfully for at least six weeks or two months, the home applications with the formojecteur being supplemented from time to time by more thorough treatments by the physician. Chemical tests have shown the formalin vapors to be absolutely neutral, so that no deleterious consequences, such as the production of sterility, are to be feared. The treatment is entirely painless, and appears to deserve a place in the realm of medical gynecology.

Formation of an Artificial Ureter.—The results of some interesting attempts to form artificially a segment of ureter from the abdominal wall are reported by STRAUSS (*Surg., Gyn., and Obst.*, 1914, xviii, 78). The work was performed on dogs, and while purely experimental as yet, may well prove to be of practical application to clinical surgery. The technique was, very briefly, to form a pedunculated flap from the transversalis muscle, fascia, and peritoneum, the peritoneum and abdominal wall being then closed, so as to make the remainder of the operation wholly extraperitoneal. The ureter was then exposed, and two or three inches of it resected; the two cut ends were then anastomosed into the upper and lower end of the flap respectively, this latter being rolled up like a sleeve, with the peritoneal surface inside, and closed with a continuous suture of fine arterial silk, which material was also used for the anastomoses. The operation was performed on four dogs, all of which survived until killed at intervals of from five and a half to seven months after operation. The findings in the artificial segment of ureter were extremely interesting: In three of the animals it had apparently functionated well, though in one a calculus was found lodged in the distal anastomosis, having the end of a silk thread for a nucleus. In the other 2 cases which functionated well no obstruction was found, but in one the artificial ureter was dilated

to form a pouch, and was associated with slight hydronephrosis. In the fourth dog a contraction was found, forming an almost complete obstruction at the lower anastomosis, with corresponding dilatation of the ureter and hydronephrosis. In every case the artificial portion of the ureter was transformed into a rigid, non-collapsible tube, which showed histologically in place of the peritoneum a typical transitional epithelium, such as is found in the normal ureter, surrounded by a thin layer of areolar tissue; outside of this, replacing the transversalis fascia, a definite layer of well organized bone had formed, with typical osteoblasts, and blood and lymph vessels. The transversalis muscle, forming the outermost coat, showed no change. Strauss thinks that the epithelium probably resulted from a proliferation of the epithelium of the ureter, the basement membrane of the peritoneum acting as a matrix for its implantation. The bone formation is to be explained, he thinks, by slight degenerative changes caused in the tissue by the irritating action of the urine, followed by partial calcification of this tissue from lime salts brought to it in the body fluids, together with the osteogenetic potentiality inherent in the particular group of muscles and fascia used for the flap. Strauss reports that he is continuing his experiments with free, non-pedunculated flaps, and has three dogs now alive three months after such operations.

Tuberculous Origin of Ovarian Cysts.—POLLOSSON and VIOLET (*Lyon Chirurgical*, 1913, x, 340) advances the theory that many of the so-called simple or serous cysts of the ovary are in reality of inflammatory origin, by far the most important type of inflammation in this connection being tuberculosis. They have observed that not infrequently ovarian cysts, showing themselves absolutely nothing characteristic of tuberculosis, occur in conjunction with tuberculous tubal or peritoneal lesions; they report, for instance, a case in which a cyst the size of an adult head, containing two liters of serosanguineous fluid, was attached to a tube showing distinct tuberculous changes, but without suppuration. Histologically, the cyst appeared to be of corpus luteum origin. In two other instances, tubal tuberculosis (producing no symptoms, but demonstrated histologically) was present, associated with bilateral ovarian cysts the size of oranges or larger. Pollosson and Violet believe that in such cases there is a distinct etiological relationship between the tubal lesion and the cyst formation, since the latter occurs only in conjunction with attenuated or slowly developing forms of tubal tuberculosis; in acute conditions the ovary apparently does not undergo the cystic change. In a second group of cases the cystic ovaries are associated with healed tubal or peritoneal tuberculosis. In the walls of the tubes of such patients there are often found small nodules containing caseous matter, occasionally the continuity of the tube may be completely interrupted, and all the pelvic organs buried in adhesions. In a case of this type operated on by Pollosson, the clinical history revealed the fact that at the age of four years the patient had had a severe attack of what had been diagnosed at that time as tuberculous peritonitis. At operation the characteristic conditions described above were found, and the ovaries were cystic. A third group comprises patients with cystic ovaries, without characteristic lesions of the surrounding organs,

but whose family history is such as to lead to a strong suspicion of a tuberculous condition. In many of these, although nothing typical is found at operation, this suspicion is subsequently confirmed by the development of tuberculosis somewhere else in the body. Polloson and Violet believe that the tuberculous inflammation acts by causing ovarian congestion, hyper-maturation of follicles, and excessive formation of atretic follicles, these conditions leading to the formation of sclerocystic ovaries, hematomas, and large simple cysts. They do not, however, believe that tuberculosis plays an etiological role in the production of true pseudomucinous or papillary cystomas.

DERMATOLOGY

UNDER THE CHARGE OF

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The Treatment of Lupus Vulgaris with Hot Air.—RAVAUT (*Bull. de la Société Française de Dermatologie et de Syphiligraphie*, 1913, No. 2), at a seance of the French Society of Dermatology and Syphilis, presented a case of nodular, non-ulcerating lupus of the jaw and ear which he had treated with great success with hot air combined with curettement. Under chloroform anesthesia the affected area was vigorously scraped with the curette and afterward cauterized with hot air at a temperature of 700° C. The eschar was detached at the end of ten days, and a month later cicatrization was complete, the scar being supple and non-retractile. About four months later a small suspicious point beneath the ear was cauterized with the hot air again. Two years later there had been no recurrence. Properly employed Ravaut thinks this the method of choice in the treatment of lupus; he knows of no other method which cures as quickly.

The Course the Virus of Herpes Zoster Takes to Reach the Nerve Ganglion.—MONTGOMERY (*Jour. Cutaneous Diseases*, March, 1913) believes that herpes zoster is an infection, and that the virus enters the lymphatics of the nerve sheath and travels from the periphery to the nearest ganglion. He thinks this theory best explains the neuralgia which often precedes the eruption; the unilateral distribution of the disease, its most frequent occurrence on the head, neck, and upper part of the trunk, the much more frequent involvement of the sensory than the motor nerves, the limitation of the eruption to one or two nerves, the partial inflammation of the Gasserian ganglion, the frequent great severity of ophthalmic zoster, and the enlargement of the lymphatic nodules along with the eruption.

Chronic Raynaud's Symptoms, Probably on a Syphilitic Basis, Associated with Livedo Reticulata.—WEBER (*British Jour. Dermat.*, March, 1913) reports the case of a married woman, aged fifty-four years, who had suffered from the symptoms of Raynaud's disease for

fourteen years, chiefly in the left foot and hand, slight gangrene of the toes of the left foot having occurred on one or two occasions. She had had retinal hemorrhages in the left eye and suffered from recurrent attacks of temporary amblyopia. All over the patient's back and most noticeably over the extensor surface of the extremities was an unusually well-marked, net-like, livid mottling of the skin. In Weber's opinion, both the Raynaud's symptoms and the livedo were probably "on a syphilitic basis," although the Wassermann reaction was negative; he also thought that the mitral stenosis from which the patient suffered favored the production of the symptoms.

The Etiology of Alopecia Areata.—SABOURRAUD (*Annales de Dermatologie et de Syphiligraphie*, No. 2, 1913) has observed, especially in women, a more or less close relationship between diseases of the genital apparatus and alopecia areata. He finds that there is a variety of alopecia which follows the menopause and even prolonged suppression of the menses. It may occur after ovariectomy, and, more rarely, in the course of pregnancy and even in the course of several successive pregnancies; this form seems to be relatively benign. In one case an alopecia supervened in a man coincidently with a double tuberculous orchitis, and it became total and permanent before a double castration was performed. Sabourraud (*Ibid.*, No. 3, 1913) has likewise observed certain chronic and grave forms of alopecia areata which seemed to be directly connected with exophthalmic goitre, growing better and worse parallel with the course of the goitre.

Hemorrhagic Erythema Multiforme with Fatal Termination.—DE AMICIS (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2) reports with considerable clinical and histological details the following unusual case of erythema multiforme: A coachman, aged twenty-five years, alcoholic and syphilitic, after long exposure to cold and rain, was seized with pain and swelling of the joints accompanied by sore throat and high fever. The face was markedly swollen, so that it was impossible to open the eyes and there was a macular eruption which became confluent, upon the face and upper extremities. Upon his admission to the hospital the patient was extremely prostrated, and the entire skin was covered with a papular eruption, most abundant upon the face and upper extremities, in part discrete, in part confluent, forming gyrate and polycyclic patches. The mucous membranes of the lips and mouth were likewise involved; they were swollen and cyanotic with hemorrhagic spots and erosions, and on the uvula and the left palatal half-arch there was an extensive necrotic lesion covered with a croupous exudate. The urine contained a small quantity of albumin. The patient complained much of abdominal pain with vomiting after his admission to the hospital, the prostration increased and death occurred two weeks later. As the result of the clinical study and the findings at the autopsy, De Amicis concludes that the case was one of idiopathic polymorphous erythema of the Hebra type, and that its severity was due in part to individual predisposition and in part to the lowering of the patient's powers of resistance by alcoholism and syphilis.

Mesothorium in Dermatology.—KUZNITZKY (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2) reports his experience with mesothorium in the treatment of various diseases of the skin, such as, carcinoma of the skin, vascular and pigmented nevi, lupus vulgaris, lupus erythematosus, etc. Round capsules of 5, 10, and 15 mm. diameter, containing 5, 10, 16 and 20 mg. of mesothorium were bound upon the part to be treated with adhesive plaster, in such a manner as to prevent shifting, and allowed to remain from forty minutes to two hours, the time depending upon the amount of mesothorium contained in the capsule and the depth of the disease. In 24 cases of carcinoma 19 were clinically cured, 2 were greatly improved, and in only one was the treatment a complete failure. In 13 cases of angioma there were no failures, and the cosmetic effect was excellent. In the treatment of nævus flammeus (portwine stain) mesothorium is to be preferred to the x-rays, radium, and carbon dioxide on account of the simplicity of its application and the certainty of its effect. In lupus vulgaris no cures were obtained, although improvement was noted. In lupus erythematosus the results of treatment in 8 cases were extraordinarily favorable.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Action of Lymph Gland Juices on Tubercle Bacilli.—MARFAN, WEILL-HALLE and LE MAIRE (*Jour. de Physiol. et de Path. gén.*, July 15, 1913, xv, No. 4) determined that the tissue of lymph nodes and of the spleen exercises an attenuating action *in vitro* upon tubercle bacilli, the liver definitely, but less so. The serum appears to exercise no attenuating effect, and the brain pulp actually an exalting effect. Marfan, Weill-Halle, and Le Maire can only offer hypothesis by way of explanation, and admit that the result may be due to the products of autolysis, and that thus the same process will not be at work *in vivo*. However, certain results have shown a parallel process in the living animal.

Changes in the Circulatory System in Acute Edema of the Lungs.—KOTOWSCHTSCHIKOW (*Zeitsch. f. exper. Path. u. Ther.*, 1913, xiii, Heft 3, 400) has undertaken a very complete series of experiments dealing with various problems relating to the power of the heart, and changes in the arterial system during and after the production of acute edema of the lungs. The most frequently observed form of general acute edema of the lungs is toxic; less often lesions of the bloodvessel walls produce an edema of a mechanical nature, while

edema of a purely neural origin is yet unobserved. Anything which prevents the flow of blood out of the lesser circulation into the left auricle may readily produce a general acute mechanical edema of the lungs, as well as anything which rapidly lessens the calibre of the lung capillaries. In such a case the pressure in the pulmonary arteries is greatly increased, as is also the work of the right ventricle, while the general arterial system, that is, the greater circulation, is apt to indicate a fall of pressure. In the human being an acute edema of the lungs may be brought about by damage to the flow of blood into the left auricle, rapidly produced by, for example, a tumor, an aneurysm, even a thrombotic formation in the vessel itself. Experimental toxic edema is readily produced by different poisons, but while it is generally accompanied by a heightened pressure in the pulmonary artery, and so increased contraction in the right ventricle, nevertheless it may exist even in the absence of these phenomena. The mechanical production of such an edema seems to depend upon an increase in the size of the pores of the lung capillaries, which the active movement of the blood increases, of which an increase of pressure in the pulmonary arteries is the forerunner. The edema which occurs in many cases after the inhalation of ether is apparently of this nature. A lowering of pressure occurs equally in the mechanical and toxic edema, while heightening of pressure, or a normal pressure on the other hand, occurs only in toxic forms. The pulse exhibits nothing characteristic; the beat may be slow or rapid, regular or arrhythmic. In mechanical edema the pulse may reflect a descent of the arterial pressure, and in any case the character of the pulse will have considerable meaning as indicating the state of the heart itself with reference to overcoming the edema. Kotowschitzshikow states that the so-called neuropathic edema as a primary occurrence experimentally produced has not yet been observed, and considers that the number of clinical observations in favor of its occurrence are not yet sufficiently numerous to allow a definite opinion upon it.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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ORIGINAL ARTICLES

**CHOLECYSTITIS WITHOUT STONES OR JAUNDICE IN ITS
RELATION TO CHRONIC PANCREATITIS.**

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CHOLECYSTITIS without stones is comparatively a common disease, and of late has come into considerable prominence. The types vary in intensity from the mild, chronic catarrhal to those characterized by necrosis of the mucous membrane, perforation, and other manifestations of severe bacterial infection.

A certain amount of uncertainty exists as to when chronic cholecystitis should be considered surgically. Not infrequently the condition is associated with appendicular infections of a chronic character, especially those forms of appendicitis in which foreign bodies, usually fecaliths, are present. Whether or not such appendicular infections are the direct cause of the infections in the gall-bladder has not been determined, but it seems possible inasmuch as bacterial or toxic products are picked up in the derivatives of the portal circulation, carried to the liver, and there destroyed or excreted in a modified form with the bile. When such infected bile is delayed in the gall-bladder, cholecystitis may result.

The clinical diagnosis of cholecystitis even when stones are present is not always easy. With the palm of one's hand, an area may be covered which could be involved in pyloric and duodenal ulcer, disease of the gall-bladder, appendicitis, and stones or infections in the right kidney or right ureter. Pain referred to this region may also be due to small ovarian dermoids and early extra-uterine pregnancy. Frequently the diagnostician must

judge as to the truth of certain alleged facts narrated by the patient not by an examination of the evidence, but by delivering judgment as to the credibility of the statements of the patient. At the time the examination is made, there may be no signs which would furnish a basis of differentiation, since the patient is not then suffering from those leading symptoms which he describes.

If these difficulties present themselves when gall-stones are actually present, how much more difficult is it to make a diagnosis of chronic cholecystitis without stones when signs and symptoms are less marked. Even when the abdomen is open, a gall-bladder markedly diseased in its mucous membrane may give little or no evidence of such disease by external examination. In an examination as to the end results of some 350 patients that had been operated on for gall-stones and cholecystitis, Stanton¹ showed that more than 90 per cent. were cured or satisfactorily improved when gall-stones were present, while in only about 50 per cent. having cholecystitis without stones were the results satisfactory.

Some operators go so far as to say that they never make a diagnosis of gall-stone disease, but tell the patient that he has "an inflamed gall-bladder which needs to be opened and drained." This makes the problem too easy and leads to "snap-shot" judgment in which bias and personal equation assume too much importance. If tarry bile, that is, dark-colored bile containing a considerable admixture of mucus, be accepted as evidence of cholecystitis, a large number of mistakes in diagnosis will not be detected at operation and a corresponding number of patients will fail to obtain relief not because of the failure of operation to cure cholecystitis, but because cholecystitis in the surgical sense was not present. This may also be true of adhesions. It should not be forgotten that so-called bands and adhesions are not limited in their development to fetal life, but are continuously forming throughout life. A band of adhesions frequently extends from the gastrohepatic omentum across the duodenum in its second portion, from the gall-bladder to the transverse colon, without causal infection in the duodenum, gall-bladder, or transverse colon, and, of themselves, such adhesions cannot be considered an indication of cholecystitis. In the later period of life there is often a deposit of fat just underneath the peritoneum of the gall-bladder which gives it a whitish appearance and a feeling of thickness to the touch without any infection of the organ itself, but which may be taken for evidences of cholecystitis. The most reliable sign of cholecystitis is markedly enlarged glands along the common duct and at the juncture between the common and cystic ducts. In cholecystitis of long standing, such lymph nodes may become calcareous. Two cases of chronic cholecystitis

¹ Jour. Amer. Med. Assoc., August 5, 1911, pp. 441-4.

were observed in our clinic in which calcareous lymph nodes compressed the common duct, producing jaundice. In both instances the patients were cured by the removal of the gall-bladder and the obstructing glands.

Chronic cholecystitis produces two types of gall-bladders: (1) The large, blue, distended gall-bladder, which does not empty itself normally under compression. The bile in the gall-bladder is thin and often foul-smelling from colon infection. (2) The thick-walled, whitish gall-bladder, which is often adherent, and contains bile usually thick and tarry, with a large admixture of mucus. In many instances the gall-bladder appears to be normal. As a rule, enlarged glands along the common duct will readily be detected. Enlargement of the lymphatics may be the only sign in some cases to indicate that the gall-bladder is probably diseased. If the symptomatic evidence that cholecystitis is present is characteristic, it becomes necessary to open the gall-bladder and examine the mucosa before a diagnosis can be definitely established. At times the disease will be limited to one area which will probably not be detected by merely opening and examining the mucous membrane. In such cases the cause of the symptoms may not be discovered unless the entire gall-bladder is removed and subjected to careful scrutiny.

Assuming the foregoing to be true, it can readily be seen that while cholecystitis without gall-stones exists, until the gall-bladder is opened its existence cannot always be determined. Even after opening the gall-bladder and exposing the mucous membrane, the diagnosis of cholecystitis in the surgical sense may remain more or less doubtful until the gall-bladder or some portion of its mucous membrane be subjected to examination by the pathologist. Fortunately, for purposes of diagnosis, the strawberry gall-bladder is one of the more frequent types of cholecystitis, the mucous membrane being covered with yellow specks as though from ulceration and deposit of gall-stone material. As a matter of fact, these little yellow specks are the base of the exposed villi of the mucous membrane, which have been stripped of their covering epithelium and their connective tissue has been stained yellow by the bile.² The disease is strictly confined to the gall-bladder. The strawberry gall-bladder is easily diagnosed on inspection of the mucous membrane. Following radical operations for this condition as high, if not higher, percentages of cures are obtained as following radical operations for gall-stones, because the common and hepatic ducts, if involved at all, will be involved only in a catarrhal process and not subjected to the traumatism of possible stones which have descended from the gall-bladder into these ducts.

Taking the strawberry gall-bladder as the type, the more varia-

² MacCarty: *Annals of Surgery*, May, 1910, pp. 651-669.

tion from it toward the normal gall-bladder the less the prospect of cure following operation because of less certainty in the diagnosis. Our scientific conscience should not be satisfied by asserting, on slender evidence, that cholecystitis exists if a diagnosis of gall-stones has been made and stones have not been found. The wish may be father to the thought and the condition should not be pronounced cholecystitis without such a diagnosis being verified by the pathologist and a grade of severity established which would make it a surgical disease. We all experience humiliation on failing to verify, at operation, a diagnosis of gall-stone disease or cholecystitis. These failures should be classified and recorded in the hospital statistics as "negative explorations of the gall-bladder." In the present state of our knowledge these are justifiable mistakes.

The milder degree of cholecystitis when subjected to operation will not present a high percentage of cures, and under existing conditions should usually be considered medical rather than surgical.

Experience teaches another lesson. While cholecystotomy may be an efficient procedure in gall-stone disease when the gall-bladder is otherwise normal and the ducts are free, in cholecystitis the method is not satisfactory. A gall-bladder which can keep up continuous trouble from infection alone without the mechanic irritation of gall-stones will probably not be cured by simple drainage, and cholecystectomy will be the procedure to follow. As a matter of fact, cholecystectomy is now largely indicated in gall-stone disease, and it may be said that practically all cases of cholecystitis and the large majority (probably 80 per cent.) of cases of gall-stone disease should be treated by cholecystectomy rather than cholecystostomy.

If so much uncertainty can exist with regard to the gall-bladder and its infections, how much more uncertainty must exist as regards the pancreas and its infections. The sense of sight cannot aid in solving the question, as in the examination of the mucosa of the gall-bladder, and a specimen will probably not be removed for pathological examination. The diagnosis must be established by the sense of touch and a certain amount of "intuition" on the part of the diagnostician, which unfortunately often plays too large a part in his final judgment. For many years I have made it a practice to examine the entire contents of the abdomen with the gloved hand whenever it was opened for any purpose and the condition of the patient would permit such manipulation. I have been surprised to find how frequently the pancreas showed enlargement, induration, and nodulation which would have justified a diagnosis of chronic pancreatitis if some disease of the biliary tract had been the original lesion, but in which there was no symptomatic evidence whatsoever that pancreatic inflammation existed.

In the routine examination of patients in our clinic, several hundreds of examinations of the stool have been made, in cases of chronic pancreatitis of this type, to try and ascertain whether or not there were symptoms of pancreatic insufficiency. Such a condition was rarely shown either in cholecystitis or in connection with gall-stone disease. It would seem, therefore, that statistics of the relative frequency of chronic pancreatitis should be accepted with some reserve. Evidence which to one would indicate chronic pancreatitis, to another might not do so. Yet that chronic pancreatitis does exist, and that it exists most commonly in connection with infections of the biliary tract, is an established fact.

The well-marked cases of chronic interlobular pancreatitis involving the head and often the entire pancreas, present conclusive evidence of pancreatitis just as the strawberry gall-bladder presents conclusive evidence of cholecystitis. Such extreme evidence of chronic pancreatitis is seldom found without infection of the biliary tract, but in cases less marked the evidence is often insufficient to establish the diagnosis, especially when neither gall-stones nor jaundice are present.

Robson³ has shown that in one-third of the cases the common duct passes behind the pancreas, so that even if chronic pancreatitis is present, the common duct is not necessarily compressed and there may be no jaundice. In such cases, however, an infection from the biliary tract may extend to the pancreas and produce chronic pancreatitis. Whether this occurs more often by mucus continuity through the cystic, common, and pancreatic ducts, or, as Deaver⁴ has shown, through the associated lymphatics, cannot always be determined.

Estimating at their full value all of these possible sources of exaggeration or error, there still remains a group of cases in which cholecystitis of a chronic type without gall-stones and without jaundice is accompanied by undoubted chronic interlobular pancreatitis. In such cases there is no dilatation of the common duct nor is the gall-bladder distended. That chronic pancreatitis is best treated by drainage of the bile tract is a lesson so thoroughly taught that even in those cases in which there is no evidence whatsoever of interference with biliary or pancreatic drainage, as shown by jaundice and distention of the common duct and gall-bladder, we still adhere to the practice of draining the gall-bladder without regard to the fact that it is the infection within the gall-bladder which has caused the disease of the pancreas, and that this infection will probably not be cured by drainage.

It is the object of this paper to show that in the presence of chronic pancreatitis without jaundice and without evidences of

³ Diseases of the Gall-bladder and Bile Duct, 1904.

⁴ Deaver: *Annals of Surgery*, xxiv, 1896, pp. 58-63.

back pressure on the biliary tract the gall-bladder should be removed if it shows marked evidences of chronic cholecystitis, especially the strawberry type.

In at least a half-dozen cases operated on in our clinic the following sequence has occurred: Cholecystostomy had been done for chronic cholecystitis without stones, and with a complicating chronic pancreatitis. The patient was relieved for some weeks or months and then the symptoms returned. Recognizing the need of more prolonged drainage, the gall-bladder was reopened and drained for a considerable period. There was complete relief so long as drainage of the gall-bladder continued, but sooner or later, after the fistula in the gall-bladder healed, the symptoms returned.

These cases are characteristic, and I have no doubt have been observed by many surgeons who have been puzzled to know just what course to pursue. It has been our experience that removal of the gall-bladder promptly relieves the symptoms and permanently cures the patient. Just what the future condition of the pancreas may be, one has no means of knowing, but I have found that chronic pancreatitis, the result of gall-stone disease, is usually cured by the removal of the stones and drainage of the biliary tract, and that in the chronic infections of the gall-bladder with secondary involvement of the pancreas, in the absence of interference with biliary drainage, cholecystectomy furnishes a satisfactory symptomatic cure.

THE TREATMENT OF PYLOROSPASM IN INFANCY.

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As early as 1788 Hezekiah Beardsley described a condition of stenosis and thickening of the pylorus occurring in young infants, and during the middle of the last century, Williamson and Dwosky also published accounts of this disease; but attention was not directed to it with sufficient force to bring it to the notice of the profession in general until Hirshsprung studied it in 1888. Since that date there have been a large number of contributions on this subject and an immense amount of theorizing as to the cause of this and allied conditions.

There is a symptom-complex not infrequently met with which is so striking that it cannot escape attention. This consists in vomiting, which is more or less projected in character, and con-

sisting of food, some mucus, and at times streaks of blood. There is constipation, or sometimes alternating constipation and diarrhea, loss of weight, a dilated stomach, visible peristalsis, and in many cases careful palpation reveals a thickened pylorus. This symptom-complex, with slight variations, may be caused by two conditions, one which may be and usually is called congenital hypertrophic pyloric stenosis, and the second pylorospasm.

The first of these conditions has been noted in autopsies of the fetus, and has been studied in autopsies on infants. It is distinctly a congenital condition, concerning which there is considerable difference of opinion. It occurs in all classes of society, affects the firstborn more frequently than any other child, and there is rarely but one instance in one family. Eighty per cent. of the cases occur in boys. The symptoms in these cases date from birth or shortly after birth.

Pylorospasm, on the other hand, may be regarded more as an acquired condition, may occur either in breast-fed or artificially fed infants, and while commonly seen from one to two weeks after birth, may be noted at any age. Pylorospasm we know chiefly by its symptomatology and the study of the living cases. There are gradations between these two classes, so that a mild case of the congenital form may have associated with it a considerable amount of spasm which intensifies the symptoms, and, on the other hand, it seems highly probable that a more or less continuous spasm of the pylorus might lead to thickening of the pyloric muscle, just as increased use of any muscle leads to hypertrophy. The outlook in these two conditions varies greatly. The well-marked cases of hypertrophic stenosis are exceedingly liable to die unless an operation is performed which will permit food to pass from the stomach, otherwise the child gradually starves to death. The pure cases of pylorospasm, particularly those coming on in late infancy, almost invariably get well, if properly treated; but there are certain cases which go on to an unfavorable termination regardless of the management.

With our present knowledge it would seem impossible to tell in every instance whether the lesion was distinctly congenital or whether it was acquired after birth. The important point from the standpoint of prognosis and treatment is to differentiate the cases in which there has been a great amount of thickening and those in which the condition is largely, if not entirely, due to spasm. This differential diagnosis cannot always be made, but there are a certain number of things which help one in making the decision. In the cases in which there is actual stenosis and thickening, the infants are constipated and the stools may even be of a character suggesting starvation. The vomiting may begin shortly after the birth of the child, and is usually, though not always, sometime after taking the feeding. The emaciation is

progressive, visible peristalsis very marked, and in most instances the enlarged pylorus is felt without any difficulty. It is a hard, unchanging mass. In the pylorospasm cases, on the other hand, there are alternating periods of constipation and diarrhea, the vomiting is usually, although not always, immediately after taking food, the visible peristalsis is not so marked, and a tumor at the site of the pylorus may or may not be felt. In some instances the tumor is felt only with peristalsis, and it may change in its size and shape under the palpating finger; when this occurs it is safe to make the diagnosis of pylorospasm, or at any rate the condition consists of much more spasm than it does of actual thickening. The pylorospasm may occur at any age. It does not always follow so definitely after birth. I have had one instance, however, in which the vomiting dated almost immediately from birth, the child subsequently making a perfect recovery.

The question of the management of these cases is one of great importance. The first point to consider is the advisability of operative procedure, and while this should be undertaken in undoubted cases of hypertrophic stenosis, and the chances of recovery of the child are better if it is not postponed too long, still in view of clinical experience with these cases, the writer thinks one should always go slowly in deciding whether one is dealing with an hypertrophy or a pylorospasm. In a certain proportion of cases in which the lesion is apparently an hypertrophic stenosis, recovery takes place without operation. Every case must be decided on its own merits, according to existing conditions. A period of from three to six weeks of medical treatment may be tried before deciding upon an operation, unless all the symptoms and signs should make the diagnosis perfectly clear before this period has elapsed. This period of waiting will generally make clear if not the actual condition, certainly the severity of it. Cases coming on immediately after birth and severe in character are much more likely to require operative interference than those which come on later and progress more slowly. The choice of operation lies between a pyloroplasty and a posterior gastro-enterostomy, and this decision may be left to the operating surgeon.

The management of these cases from the medical standpoint is extremely important. The first point of importance is the feeding and there can be no question whatever that these patients, and we refer particularly to pylorospasm, do better on breast milk than upon any other food that can be found. In severe cases occurring in young infants every effort should be made to obtain human milk. This point cannot be emphasized too strongly. If the mother's milk contains a great deal of fat, it may be allowed to stand and some or all of the cream removed. There is considerable difference of opinion as to the effect of the fats in feeding these cases, and it seems to me there is considerable variation in the cases in regard to this. If the case is not doing well, it certainly

is not amiss to remove the fat, at least temporarily. I should not consider using any other form of feeding than human milk or some slight modification of it unless circumstances absolutely prevent securing it. When it cannot be obtained in sufficient quantities, more or less completely peptonized cow's milk may be substituted for part of the feeding. This milk may be one part cow's milk and three parts water, or one-third cow's milk and two-thirds water, peptonized from five to twelve minutes, or the weaker percentages of modified milk may be used; if these fail, well-diluted malted milk or condensed milk diluted with water, in a proportion of one to ten or one to twelve may be tried. In the severe cases in which practically everything is vomited, the food should be given by means of a stomach-tube, as it is much more liable to be retained when given in this way than if the baby be allowed to nurse the breast or to take the milk from a bottle. There are curious things in regard to the retention of food, two of which deserve special mention: one is that with any change of food there is retention of the food for two or more feedings, and sometimes eight, twelve, or sixteen hours elapse before the vomiting recommences. The second point is that sometimes several feedings are taken one after the other, the stomach becoming more and more dilated, and finally the total quantity of food vomited hours afterward. The use of the tube for feeding obviates putting milk into an already filled stomach. The frequency of feeding is a matter of considerable importance, and will depend upon the amount that can be given. Most of these babies will retain small feedings longer than larger ones, but I think it is a good plan to gradually increase the size of the feeding, giving as much as can be retained. If the feeding is a little too large it will be rejected, but a competent nurse can usually determine the size of the feeding after a little experience with any given child. Two hours should perhaps be the greatest interval that should be allowed to elapse between the feedings, and in some cases this interval may be shortened to considerable advantage. Occasionally, longer intervals may be resorted to temporarily, but not as a general rule. The child should be kept flat on its back immediately after the feeding, and not handled any more than is absolutely necessary. In this connection it is hardly necessary to add that the child should be kept in a perfectly quiet room and not disturbed by visitors and friends or any other members of the family.

The stomach should be washed out once or twice a day or oftener, varying the frequency of the lavage according to the amount of mucus present, and it is sometimes advisable to use a bicarbonate of soda solution, one dram to the pint, in cases where the mucus is thick and stringy or where the vomitus is intensely acid. Other foods than those mentioned above have been suggested, particularly beef-juice and the white of egg and water, or the use of cow's milk with sodium citrate. The meat and the egg we should

regard as doubtful expedients, as neither is adapted for more than the most temporary feeding, and even that on a starvation basis. Rectal feeding may be used in bad cases, but in my experience the administration of food by rectum in young infants is not a satisfactory method of feeding, although there is no doubt that even the small amount that can be thus given and absorbed is of distinct value. The use of the rectal administration of plain water or in some instances of salt solution is, however, of the greatest benefit, and may be used in all cases where the amount of fluid vomited is very great. It relieves the thirst of the child and stimulates excretion of the urine.

Another point of importance is to maintain the body heat. The temperature of the child should be taken and hot-water bags or other devices used as may be necessary. Occasionally there may be a certain amount of febrile disturbance, particularly when the starvation begins to be manifest.

Counter-irritation over the epigastrium has been suggested, particularly by German writers, and this is usually accomplished by means of weak mustard plasters, spice bags, or by some form of a warm application. Too much need not be expected from this procedure, but there is no reason why it should not be tried.

The question of the use of drugs in these cases is one about which there has been considerable written. In my experience, atropin is so far superior to any other form of medication, and I unhesitatingly recommend it as the first thing to try, giving it in doses of $\frac{1}{2000}$ grain at intervals of four to six hours, and sometimes even at shorter intervals. This dose may be reduced if it produces symptoms of belladonna poisoning, but I have never seen this amount cause any such trouble. If no therapeutic effect is obtained after a reasonable trial, the dose may be cautiously increased until the first symptoms of the drug are noted. As soon as this is seen, the amount may be diminished and the smaller doses, if found useful, may be continued even over a considerable length of time. Opium in the form of the deodorized tincture has its warm advocates. Codein may be tried in place of opium. When codein is used, $\frac{1}{800}$ grain may be administered at the start, and the amount increased cautiously. If the deodorized tincture is preferred, $\frac{1}{40}$ minim may be the starting dose. Sodium citrate, bismuth subnitrate or other bismuth preparations, alkalies, and acids have all been suggested, but are of exceedingly questionable value.

SUMMARY. The points to which I have particularly called attention are:

1. A more careful diagnosis.
2. A longer trial at medical treatment, especially in all cases in which the diagnosis of pylorospasm is probable.
3. The necessity of the use of breast milk.
4. The superiority of atropin to other forms of medication.

TUBERCULOSIS OF THE SPLEEN, SEPTIC INFARCTION, POLYCYTHEMIA. SPLENECTOMY.

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SECONDARY tuberculosis of the spleen is not uncommon. True primary tuberculosis of the spleen is probably extremely rare. In the cases of so-called primary tuberculosis of the spleen described in the literature the tuberculous process in the spleen forms the main lesion, the probable original focus or point of entry, in the lungs or lymph nodes, for example, remaining quiescent or becoming healed, while the process in the spleen develops, and is the cause of the symptoms presented by the patient.

The first case of primary tuberculosis of the spleen was reported from autopsy by Coley¹ in 1846. The first reported splenectomy for splenic tuberculosis is that of Burke² in 1889. The patient died the following day, apparently from sepsis. No autopsy was performed in this case, but previous physical and sputum examination showed no evidence of pulmonary tuberculosis. In 1898 Quenu and Baudet³ collected and reported five cases, including one of their own. In 1899 Rendu and Widai⁴ described a symptom-complex including tuberculosis of the spleen, polycythemia without leukemia, and cyanosis. They attributed the symptom-complex to the splenic lesion. Bayer⁵ collected, up to 1900, 9 operations with 7 recoveries, including 1 of his own, and 19 autopsy cases. He emphasizes the importance of splenectomy, and also the relative diagnostic importance of polycythemia and cyanosis. His patient had 6,000,000 red cells, 7500 white cells, hemoglobin 40 per cent., and was pale. G. B. Johnson⁶ in an article on splenectomy published in 1908 included reports of ten cases of splenectomy for tuberculosis, with two deaths.

The most recent and complete article on this subject is that by Winternitz,⁷ who has collected and tabulated 51 cases from the literature; 16 of these cases have been operated on, 9 cases recovered (56 per cent.). The list includes 3 cases; 1 by Ciaccio,⁸ in which

¹ Trans. Path. Soc., London, 1846, i, 276.

² Dublin Jour. Med. Sci., 1889, xlvii, 540.

³ Rev. de gynéc. et de chir. abd., 1898, ii, 317.

⁴ Bull. et mém. Soc. de Med. des hôp., 1899, Series 3, xvi, 528.

⁵ Mitt. a. d. Grenzgeb. d. med. u. chir., 1904, xiii, 523.

⁶ Ann. of Surg., 1908, xlviii, 50.

⁷ Archiv Int. Med., 1912, ix, 680.

⁸ Deutsch. Zeitsch. f. Chir., 1909, lviii, 464.

splenectomy was not done on account of adhesions; 1 by Hayden,⁹ in which the spleen was sewed to the abdominal wall and drained; and 1 by Hamilton,¹⁰ in which the same procedure was carried out. His analysis and summary of the 51 cases is so thorough and complete that the conclusions found as a result of his study may be given here as follows:

Tuberculosis of the spleen seems to be equally frequent in the male and female sex. It is most frequent between the ages of twenty and forty, but may occur at any age, the youngest in his tabulated list being one year, the oldest eighty years. The symptoms may run an acute or chronic course, in the acute cases the symptoms were those of an acute systemic infection, and in the chronic cases the onset was characterized by pain or tumor in the splenic region (70 per cent. of cases). There may be, in addition, gastro-intestinal or respiratory disturbances. In the list of 51 reported cases the blood count was given in 26. It was normal in 9 (34.61 per cent.), and showed anemia in 11 (42.30 per cent.); polycythemia was present in 6 (23.08 per cent.). The anemia was not marked in any instance, 3,200,000 being the lowest count. As a rule the leukocytes were not increased, and their number seems totally independent of the number of red cells. In his conclusion, Winternitz states that "death invariably follows if the spleen is not removed."

In contrast to this statement of Winternitz we have the statement of Osler¹¹ in an article on Erythrocythemia, "Splenectomy should never be done in these cases." And the list of reported cases in which the blood picture shows a true polycythemia bears out this latter conclusion. In view of the fact that in our case tuberculosis of the spleen and polycythemia co-existed, these conflicting statements make the question of the treatment of such cases a difficult one. Owing to the apparent relationship between tuberculosis of the spleen and polycythemia it may be of interest in this place to consider briefly what is known of polycythemia, excluding those cases due to change in altitude or chronic coal-tar products poisoning:

Polyeythemia as a definite disease was first described by Vaques¹² in 1892. Osler¹³ in 1903 and Turk¹⁴ in 1904 brought the syndrome into general notice (enlarged spleen, cyanosis, and high red-count), with early case reports by McKeen¹⁵ and Saundby and Russell.¹⁶ Since then so many cases have been reported in the literature that in 1911 Watson Wemyss,¹⁷ in a review of the subject, cites sixty references.

⁹ Trans. Indiana State Med. Soc., 1897, xlviii, 96.

¹⁰ Internat. Clin., 1896, vi, Series 3, 213.

¹¹ Principles and Practice of Medicine, 1912, Eighth edition, 757.

¹² Compt. rend. Soc. de biol., Paris, 1892, xlv, 384.

¹³ AMER. JOUR. MED. SCI., 1903, cxxvi, 187.

¹⁴ Boston Med. and Surg. Jour., 1901, 144.

¹⁵ Edinburgh Med. Jour., 1911, vol. vi.

¹⁴ Wien. klin. Woch., 1904, xvi, 153.

¹⁶ Lancet, 1901, i, 515.

There are five theories as to the etiology of polycythemia: (1) That the disease is a primary myelopathy (Parks Weber),¹⁸ and Jacobs¹⁹ writes of the disease as a neoplasm of the blood similar to a neoplasm of the tissues in cancer; (2) splenic tuberculosis (Rendu and Widal²⁰ and Lefas);²¹ (3) diminished destructibility of the red blood corpuscles; (4) diminished oxygen-carrying power of the hemoglobin (Bence);²² (5) theory of blood-stasis, the extreme viscosity of the blood being a marked phenomenon in these cases of polycythemia.

The above brief review of the literature on the subject is enough to indicate how little really has been definitely determined as to the etiology and essential pathology of polycythemia. Moreover, the direct relation between polycythemia and tuberculosis of the spleen is open to question. Therefore, while the multiplicity of lesions demonstrated by autopsy, in the following case, prevents definite conclusions, the history, report of operation, clinical data, and report of autopsy are presented as a contribution to the literature on the subject.

For much of the previous history of this patient, and for the clinical data extending over a period of seven years, we are indebted to Dr. J. A. Travell, of New York.

CASE I.—J. R. S., aged thirty-nine years; salesman; born in United States.

Family History. Mother died of nephritis, otherwise irrelevant.

Previous History. Had chills and fever when a child; in youth had frequent severe nose-bleed, but in 1901 an operation for abscess in the inguinal region was not accompanied by unusual bleeding. In 1902 had pneumonia, followed by pleurisy. Was formerly a hard drinker, but later a total abstainer. Had always been constipated. Normal weight was about 180 pounds.

History taken in 1905 stated that there had been no recent cough, catarrh, or pleurisy. During the previous year he had begun to have frequent attacks, in which his face turned purple, and he became nervous, but never lost consciousness. At that time he was recovering from an attack of nervous prostration, and was troubled with indigestion and spots which flickered before his eyes. He, however, had no headache. Weight was then 147½ pounds. Physical examination showed right kidney palpable; heart lungs, and urine normal; face flushed. Intense congestion of all mucous membranes, but legs and body pale.

January, 1907. For a period of three weeks had had momentary attacks of complete blindness of the right eye from one to six times a day. An oculist reported the eyes were normal and that the

¹⁸ Quarterly Jour. Med., 1908, vol. ii.

¹⁹ Münch. med. Woch., 1912, lix, No. 44.

²⁰ Loc. cit.

²² Deutsch. med. Woch., 1906, xxxii, 1451.

²¹ Paris Thesis, 1903.

trouble was due to vasomotor disturbance. All capillaries of the body were intensely congested. Was always constipated.

April 6, 1908. Extreme capillary congestion of the face and mucous membrane of the mouth. Color below the neck was normal; feet were cool. Had epigastric pain at times, with gas in the stomach. Heart was normal; radial and temporal arteries were hard. Spleen was palpable one inch below ribs on deep inspiration.

April 8. A gall-stone was passed after severe pain for twenty-four hours. Stone was not recovered. Hemoglobin, 90 per cent.; polynuclear leukocytes, 88 per cent.; transition leukocytes, 1 per cent.; eosinophiles, 2 per cent.; small lymphocytes, 5 per cent.; large lymphocytes, 4 per cent.

April 22. Face was flushed as usual. Abdomen was not sensitive. Liver dulness was normal. Spleen was not palpable.

May. Face was scarlet. Spleen was barely palpable below the ribs. No hepatic tenderness; no gastric splashing. Drinking buttermilk invariably caused blindness and dizziness in half an hour, the attack lasting twenty minutes.

June. Face was constantly flushed; weight, 146½ pounds. Spleen not palpable; heart, lungs, and abdomen were negative. Reflexes were present; blood-pressure, 140 mm.

July. Spleen not palpable, lacked ability to concentrate attention on work. Face was scarlet.

January, 1909. Had been well, but had frequent lapses of memory, and the face flushed annoyingly.

February. Urine examination showed albumin, acid; no sugar; granular and hyaline casts; many pus cells and spermatozoa. Quantity, two quarts in twenty-four hours. Pulse, 93 and regular, blood-pressure, 130 mm. Marked gastric splashing.

March. Had severe hemorrhage; about one quart from the bowels, immediately followed by about one quart from the stomach; both clotted heavily. Collapse; pulseless; soreness at lower left border of the stomach. The following day pulse was regular, of fair quality. No further hemorrhage. Urine, ninety-six ounces in twenty-four hours. No sugar, no albumin, many casts. Two days later the blood-pressure was 140 mm.

April. Frequent neuralgic pains in superficial vessels of the calves of the legs, lasting about five minutes. Veins distended. Face flushed, and dizzy at times. Blood-pressure, 110 mm. Weight, 145½ pounds.

May. Felt well; passed about three quarts of urine in twenty-four hours.

August. Face and hands flushed and cyanotic. Blood-pressure, 130 mm. Gastric splashing. Often lost control of himself. Slept poorly.

October. Had felt unusually well for some time. Blood-pressure,

135 mm.; weight, 152½ pounds. When badly constipated had spells, during which he momentarily lost consciousness.

June, 1910. Departed for the West. Had a good year and, as a rule, felt well. Blood-pressure, 140 mm. Heart and lungs were negative. No aneurysm. Urine showed trace of albumin; much indican. Not any blind spells.

October. While in Portland, Oregon, the patient had another severe hemorrhage, both from the stomach and bowels, and came under the care of Drs. J. O. E. King and Jones, of Portland. After this attack a careful clinical examination was made of stomach contents, stools, and blood. The gastric analysis and stool examination were negative. Blood-pressure was between 100 and 120. Leukoeytes, 32,000; red cells, 6,000,000. Weight, 148 pounds. During the interval between this attack and the year 1912 he remained in the West and did no work on account of his health. He was bled once, with relief of his symptoms. While in the Battle Creek Sanatorium during this time his blood examination was red cells, 6,550,000; hemoglobin, 92 per cent.; leukocytes, 41,000. Percentage of polynuclear cells was not given. His blood-pressure was then about 120.

In the spring of 1912 he returned to New York and resumed his occupation, and reported himself in fairly good health. Six weeks before his admission to St. Luke's Hospital, November 27, 1912, he had been suffering with indigestion and some pain in the region of the spleen. He stated that eight days before, while on a business trip, after a ride of thirty miles in a wagon on two successive days over rough roads, this pain became more severe, extending to the epigastrium. Everything he ate caused excruciating pain. He did not vomit, but felt nauseated. For several days his bowels did not move. He was then seen by Dr. Egbert Le Fevre, of New York. His chief complaints at this time were severe pain in the left hypochondriac region, radiating toward the midline and across the abdomen, extreme weakness, and a feeling of fulness in the head. His temperature was 101°.

Physical Examination. The physical examination of the lungs was negative. There was an indistinct systolic murmur at the apex. Pulse in the right radial only slightly above normal in rate. Pulse in left radial absent. The spleen was palpable about three inches below the free border of the ribs, and extremely tender. A blood-count showed between 30,000 and 40,000 leukocytes, with 92 per cent. of polynuclear cells. Two days later he was seen in consultation by one of us, his condition having remained the same, except for an increased elevation of temperature and extreme difficulty in moving the bowels (only once in three days). He was then referred to St. Luke's Hospital for observation. His temperature on admission was 103°; pulse, 100; respiration, 26. His leukocytes were 23,000; polynuclear cells, 92 per cent.

At 10³⁰ P.M. on the night of admission he had a severe chill, and one hour later his temperature was 105.3°; pulse, 148; respiration, 34. Leukocytes, 39,000; polynuclears, 95 per cent. His urine showed albumin, leukocytes, and a few red cells. Believing that he had an abscess or some septic process in the spleen, an immediate operation was advised.

Operation. An incision about 20 cm. long was made along the outer border of the left rectus muscle, and the spleen was found studded with small white areas which looked like tubercles or miliary abscesses; there was also a large softened area, evidently an infarction. The spleen was only moderately adherent, and no tubercles were seen elsewhere in the peritoneum. The liver was apparently normal. A splenectomy was done with little difficulty. The lower end of the wound was closed, the upper part being left open to allow the packing and drainage with a Mikulicz drain of the upper part of the space left by removal of the spleen, from which there was a moderate amount of oozing caused by separation of the adhesions.

For the first four days following the operation the patient's temperature averaged from 100.2 to 101.4; pulse, 116 to 128; respiration, 32 to 48. Urine showed albumin and casts. Blood picture: Red blood cells, 8,800,000; hemoglobin, 120 per cent.; white blood cells, 80,000; polynuclears, 96 per cent. A few normoblasts were found, and also aniso- and poikilocytosis and polychromatophilia.

On the fifth day the patient appeared better. Temperature, 100° to 102.2°; pulse, 116 to 128; respiration, 30 to 36; red blood cells, 7,000,000; hemoglobin, 120 per cent.; white blood cells, 21,300; polynuclears, 92 per cent.; three normoblasts in two hundred cells. Bowels moved twice.

On the sixth and seventh days the general condition about the same. Blood pressure, 117. Wound dressed, and appeared in good condition. Packing removed and a rubber dam drain inserted.

On the eighth day the temperature in the morning was 100.4°; pulse, 116; blood-pressure, 118; red blood cells, 7,600,000; hemoglobin, 120+ per cent.; white blood cells, 18,000; polynuclears, 96 per cent.; five normoblasts in one hundred cells. In the evening the patient complained of abdominal pain and felt chilly. At midnight the temperature was 100.4°; pulse, 148.

December 6, the ninth day after operation, patient's condition was worse. Temperature, 104.4°. Complained of severe abdominal pain; vomited at noon. Red blood cells, 7,400,000; hemoglobin, 120 per cent.; white blood cells, 23,000; polynuclears, 88 per cent. In the evening he rapidly became worse; his pulse became almost imperceptible. Rallied after intravenous infusion of saline solution. Asked for bed-pan; bowels moved. Two hours later pulse again rapidly became worse, and the patient died.

This long history is given in detail because of the number of curious facts that may be to some extent explained by the autopsy findings.

Autopsy No. 941. Because of the length of the article the autopsy findings are given in abridged form, with the omission of portions that do not seem to have a direct bearing upon the case.

Body of a poorly nourished adult male. In addition to the usual postmortem lividity there were irregular areas of dark, purplish color over the limbs and trunk, and also on the ears and cheeks. Abdomen considerably distended. Operative incision as previously described. Small amount of brownish, foul-smelling fluid free in the peritoneal cavity. Parietal peritoneum showed glistening surface, except in left hypochondrium, where the diaphragmatic and parietal surface over a region corresponding to the previous location of the spleen was thickly studded with small, raised, grayish-white nodules. The spleen had been removed at operation. The omentum was loosely adherent at the line of incision and around the pedicle of the spleen. Its color was dark and hemorrhagic. Vessels were considerably dilated. No thrombosis found.

Intestines: The intestines were markedly distended and the walls were completely relaxed. Serous surfaces had lost all glistening appearance. Color was dark reddish brown throughout the entire extent. Musculature and mucosa were softened and necrotic. Tissues of mesentery of the same dark color and quite swollen. No signs of obstruction or thrombosis in the vessels in the mesentery. The necrosis involved the entire intestinal tract except the sigmoid and rectum, but it was further advanced along the regions supplied by the superior mesenteric artery. The retroperitoneal glands were slightly enlarged and dark in color.

Stomach: Externally the organ showed a similar dark brownish color, but its musculature was not necrotic. The mucosa at the pyloric and cardiac extremities appeared congested, and showed some ecchymotic spots, while a band of softening about 12 cm. in width, with loss of mucosa in small areas, extended completely around the middle of the organ. No thrombosis found in gastric vessels. The organ was considerably dilated, and contained a large amount of brownish, foul-smelling fluid.

Pancreas: The surrounding and interlobular tissues were edematous, and of a dark brown color. The tail bore the structures ligated with the pedicle of the spleen. There was no evidence of hemorrhage nor of thrombosis of these vessels.

Liver: Color was dark reddish, mottled irregularly by lighter yellowish areas. Capsule was thin and smooth, except for some fibrin flakes along the left anterior margin. It measured 25 x 23 x 8 cm. Weight, 2610 gm. On section the consistency was about normal, and the cut surface presented the same yellowish, mottled appearance. A few small whitish-gray nodules resembling tubercles were found.

Kidneys: Except for their dark congested appearance and some clouding of the parenchyma the kidneys appeared normal.

Pericardium: The pericardium contained a slight excess of clear, yellowish fluid. Surface everywhere was smooth and glistening.

Heart: Subpericardial fat was small in amount. The organ appeared somewhat larger than normal. The right ventricle and auricle were distended. The apex of the left ventricle appeared rather fibrous and the color was paler than elsewhere. The right auricle and ventricle contained rather firm postmortem clots. Tricuspid valve admitted three fingers. Leaflets were smooth. The wall of the ventricle was 0.4 cm. thick. The mitral valve admitted two fingers easily. The leaflets appeared normal. The apex was occupied by what appeared from the interior as a large

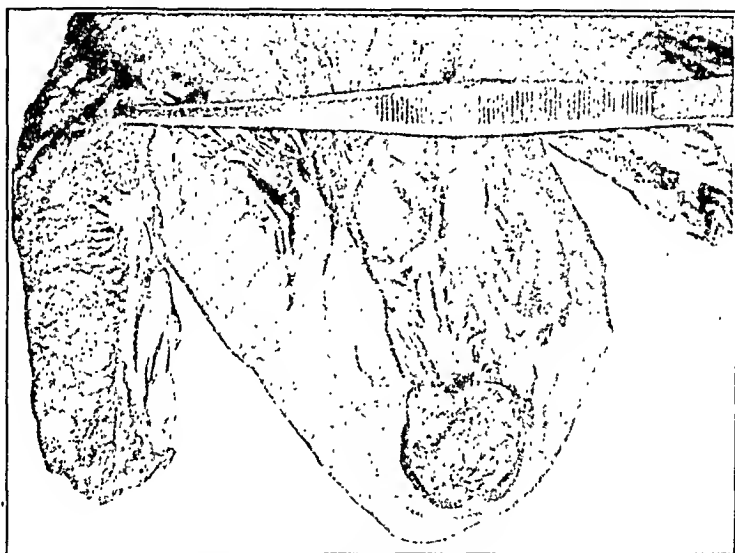


FIG. 1.—Lesions at apex of left ventricle.

mural thrombus, but which on section was evidently a subendocardial process of considerable duration. The muscle was thinned out to about 2 mm. in thickness over it, and internal to this was a dense whitish fibrous stratum about 2 mm. in thickness. Internal to this was a mass of what appeared to be softened thrombus formation. The endocardium from the lateral surface of the cavity appeared to have extended over this mass for a short distance. The diameter of this lesion was about 2.5 cm. At the point of junction of the left posterior and the anterior aortic leaflets was a fresh vegetation, with a narrow pedicle about 3 mm. long. The coronary arteries showed slight thickening and occasional patches of yellow atheroma.

Lungs: Both lungs were considerably congested, but fairly well aerated. Pleural surfaces were normal, except at the right apex

posteriorly, where a few fresh fibrinous adhesions were found. On section the upper lobe showed many conglomerate tubercles toward the central part of the lobe. These showed beginning caseation. A few rather large discrete tubercles were found in the upper right lobe. Apparently the process was a fairly recent one. The bronchial mucosa was slightly inflamed throughout, and a small amount of mucopurulent exudate was present in the larger branches. Bronchial lymph nodes considerably enlarged and showed areas of caseation.

Arteries: At the base the aorta showed numerous areas of well-advanced atheromatous degeneration without calcification or ulceration. The process was marked around the orifices of the

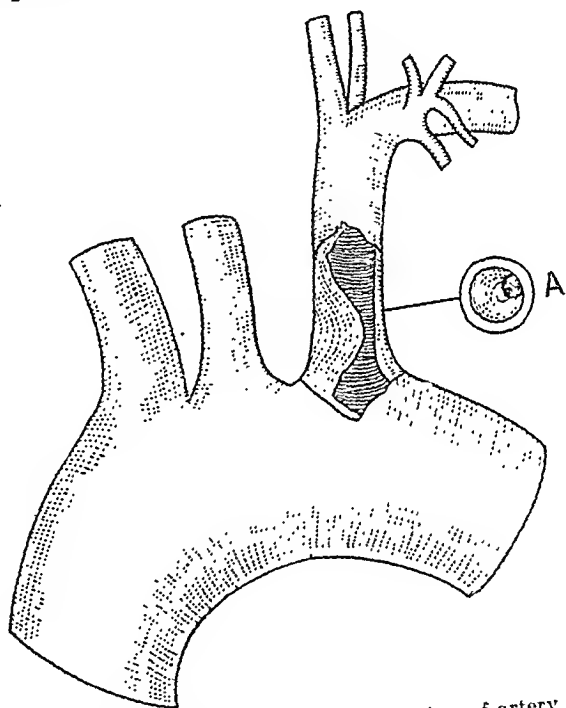


FIG. 2.—Lesion in left subclavian artery. A, Cross section of artery at point indicated.

innominate and left carotid. At the base of the subclavian artery, and extending upward for 1 cm., there was a concentric thickening of the wall, particularly on the inner anterior portion, that narrowed the lumen down to less than 2 mm. The process appeared to have been intramural rather than a canalized thrombus. The descending and thoracic portions of the aorta showed numerous plaques of yellow atheroma without ulceration or calcification, and there was a marked increase in the thickness of the arterial wall in these areas. On the posterior wall of the abdominal aorta there was an ulcerated, calcareous plaque about 1.5 cm. in diameter, to which a firm thrombus was attached. This thrombus extended into the orifice of the superior mesenteric artery, and its upper extremity

was in such a position that it could overlies the orifice of the celiac axis. The renal arteries were unaffected. The atheromatous process was present in the form of scattered plaques well down into the iliac arteries. At the bifurcation there was a firm "straddling" thrombus that extended into the iliacs for about 1 cm.

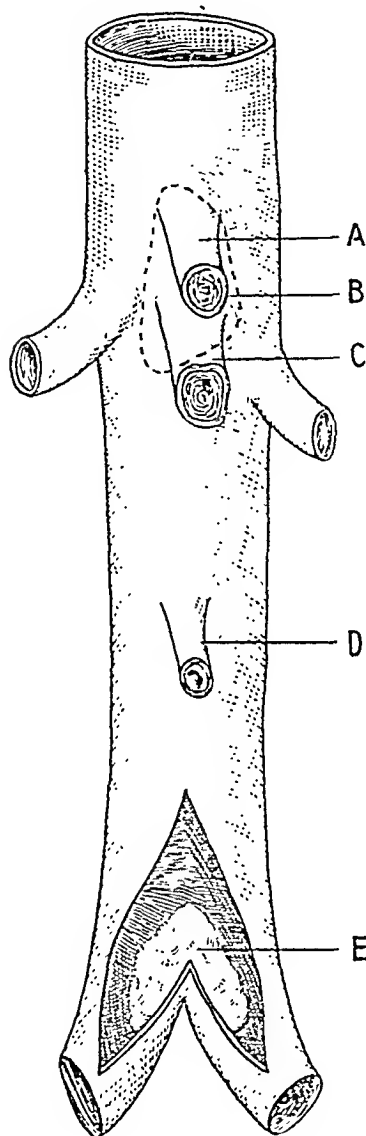


FIG. 3. — Lesions in abdominal aorta; A, obliterated lumen of celiac axis; B, location of thrombus on posterior wall of aorta; C, partial obliteration of lumen of superior mesenteric artery; D, partial obliteration of lumen of inferior mesenteric artery; E, thrombus at bifurcation of aorta.

The superior mesenteric artery was considerably sclerosed at its base, and about 0.7 cm. above this the wall was concentrically thickened so that the lumen was constricted to a diameter of 1 mm. The process appeared to be a fibrosis. Beyond this point the lumen was of normal diameter and the various branches were unobstructed. A similar, but less marked, process was present in the inferior mesenteric artery. At the beginning of the celiac axis the fibrosis was complete, and no lumen was made out. These lesions were found after removal of the organs, and it was not possible to ascertain the nature or extent of any collateral circulation that may have existed.

On opening the femur the bone-marrow was found to be of a dark grayish-red color and of soft consistency.

Anatomical Diagnosis. Gangrene of the intestines with peritonitis; thrombosis of the aorta, superior mesenteric and common iliac arteries; obstructive arteritis of celiac axis, superior and inferior mesenteric and left subelavian arteries; tuberculous peritonitis; pulmonary tuberculosis; tuberculosis of the liver; parenchymatous degeneration of the liver and kidneys; endocarditis, acute vegetative; atheroma of arteries; hyperplasia of bone-marrow. Smears from the lungs and bronchial glands showed a few tubercle bacilli. Material from the lesion in the apex of the heart inoculated into guinea-

pigs produced typical tuberculous lesions from which tubercle bacilli were recovered.

REPORT ON THE SPLEEN. Diagnosis: Tuberculosis and Infarction of the Spleen. *Macroscopic Examination:* Specimen consisted

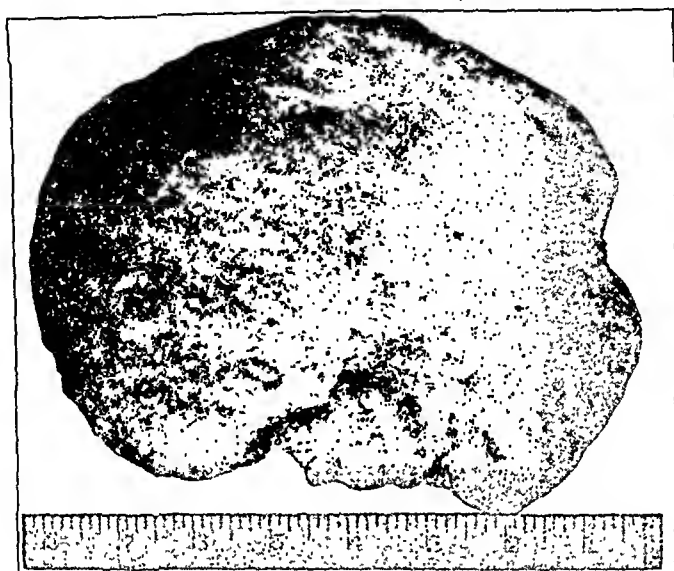


FIG. 4.—Spleen, after hardening.

of a spleen, weight 1350 grams, 22 x 14 x 9 cm. Surface was rough and nodular, with many small (1 to 3 mm.) yellowish areas scattered over the entire spleen. Capsule was thickened, and showed numer-

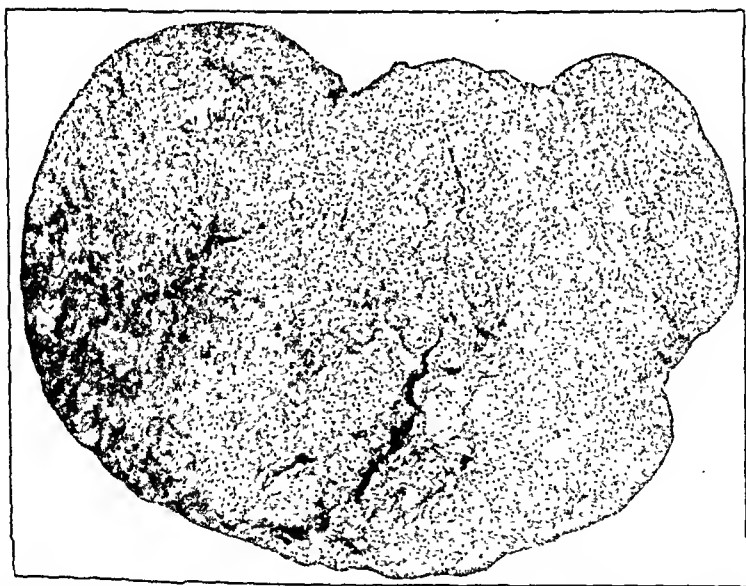


FIG. 5.—Horizontal section of spleen, after hardening, showing areas of tuberculosis and wedge-shaped infarction.

ous adhesions. Opposite hilum is an irregular area 6 x 8 cm. in diameter, much softened, over which the capsule was broken.

Cut surface was red, with innumerable yellowish areas as on the surface; these were firm and fibrous, not caseous. Soft surface area corresponded to triangular infarct extending in 8 cm.; soft fibrous, no yellowish areas. Shades off gradually through hemorrhagic zone into rest of splenic tissue.

Microscopic Examination: Small yellowish areas seen in gross are necrotic tissue, about these were zones of epithelioid proliferation and numerous giant cells of Langhans type. Fibrous tissue of spleen considerably increased. Tissue in infarcted area was entirely necrotic. Small areas of pigmentation were scattered about. No tubercle bacilli were demonstrated in section.

Microscopic Examination. Lungs: The lungs showed marked congestion of the interstitial tissue, and in some areas the alveoli were filled with red blood cells. Small discreet tubercles were numerous; many had coalesced and showed necrosis and caseation. Giant cells were particularly numerous. The smaller bronchi showed slight swelling and desquamation of their epithelium.

Bronchial Glands: Showed typical tubercle formation, with numerous giant cells of the Langhans type. Caseation was only slightly advanced. The proliferation of cells of the epithelioid type was marked. Anthracosis was present in moderate degree. The vessels were congested.

Liver: Showed pronounced congestion and a diffuse degeneration of parenchymatous cells. Many cells of endothelial type were deeply pigmented. Areas showing extravasation of blood and necrosis of the liver cells were numerous. Scattered throughout were numerous tubercles, some of which were undergoing caseation.

Kidneys: There was a moderate degree of cloudy swelling of the tubular epithelium. The glomerular tufts showed congestion and swelling of the epithelium. There was no exudate, and the capsules were not thickened. A few glomeruli were completely fibrosed, and there were a few scattered areas of interstitial fibrosis. The vessels appeared to be of normal thickness.

Diaphragm: The inferior surface in the region of the spleen showed a diffuse tuberculous process. Giant cells were numerous. A few typical tubercles were present.

Heart: Section from lesion in apex of heart showed a slight edema beneath the epicardium and a marked thickening of the walls of the arteries in this region and in the underlying muscularis. There was a slight increase of connective tissue between the muscle fibres, which were also separated by edema. About one-half of the normal thickness of the myocardium was replaced by a firm, almost hyaline fibrous tissue that had a laminated appearance and contained few nuclei. Between the muscle and this fibrous layer was a narrow zone containing many small round cells. Internal to the fibrous zone there was a mass of soft red thrombus with no evidence of organization present. In a few areas small groups

of polynuclear leukocytes were found. In one portion of the wall of the lesion there was an arrangement of the fibrous tissue in whorls that was suggestive of the fibrosis of an old tuberculous area, otherwise there was no evidence that the lesion was due to tuberculosis.

Arteries: Sections through the constricted portion of the superior mesenteric and left subclavian arteries showed a subintimal fibrous tissue hyperplasia that by concentrically thickening the wall of the vessels had markedly encroached on the lumen. In the section from the subclavian artery there was a well-marked round-cell infiltration between the area of fibrosis and the musculature, but there were no giant cells or tubercle formation.

Bone-marrow: Smears from the marrow of the femur showed the usual forms of marrow cells and an abundance of normoblasts. Normal red blood cells composed about one-third of the smear. There was practically no fat present.

A review of the history of this case for the purpose of ascertaining the sequence and possible etiology of lesions gives but little aid. From a clinical standpoint the existence of the marked polycythemia was the most interesting feature of the case. The tuberculous lesion in the spleen would seem to offer a simple explanation for this, and, in fact, attention was called to an enlargement of this organ as early as 1908, although it was not until October, 1910, that a polycythemia was demonstrated. The symptoms of flushing and congestion of the face, which continued intermittently throughout and which may or may not have had a possible cause in the polycythemia, began three years before, in 1905. Moreover, repeated examinations of the heart and lungs from 1905 until the final illness failed to reveal either a circulatory or pulmonary lesion, nor was any other evidence of tuberculosis noted.

Since primary tuberculosis of the spleen is rare, it would be reasonable to expect that some evidence of a more probable primary focus in the lungs would have been manifested. The history of pneumonia with pleurisy in 1902 is suggestive as a possible starting-point for a pulmonary focus, but the autopsy did not seem to indicate a pulmonary lesion of such long standing. However, if one wishes to regard the marked diffuse tuberculosis of the spleen as the cause of the polycythemia, a sufficiently reasonable sequence of events is present on which to base an assumption of such an etiology.

Many of the symptoms referable to disturbance of the digestive tract are readily explained, if it be agreed that the lesions found in the walls of the arteries were of ten years' duration. The various attacks of "indigestion," dizziness, blindness, and the two attacks of hemorrhage could be regarded as caused by an interference with the blood-supply of the digestive organs. In spite of the fact that the second hemorrhage was attributed to high blood-pressure,

and that venesection apparently relieved certain other symptoms, there is no record of a pressure above 140 mm. The vascular lesions must certainly have been of long duration and of a development sufficiently slow to permit of the formation of an extensive collateral circulation. The completeness of the obstruction of the celiac axis and mesenteric arteries permits of no other supposition. The lesions themselves offer little suggestion as to their origin, or to any etiological association with the polycythemia. The lesion in the apex of the left ventricle appeared to be of the same general nature and age as those in the arteries.

Whether the final attack beginning in October, 1912, was precipitated by a lighting up of an old pulmonary tuberculosis, or whether the failing blood-supply to the spleen caused a dissemination of its tubercle bacilli and a starting-point for an acute infectious process, must be left to conjecture. The most obvious cause of death was the gangrene of the intestinal tract, which must be attributed to the lesions found in its arterial supply.

Obviously there is little possibility of any inferences being drawn as to the result of operation in cases of tuberculosis of the spleen or of polycythemia, from our experience in this case. Of course, the autopsy findings demonstrating the obliterative arteritis of the celiac axis and superior mesenteric vessels resulting in gangrene of the intestines and causing death showed plainly the futility of any therapeutic measures in this particular case. And if this arteritis had not caused an early fatal termination, the lesion in the apex of the heart with its thrombus, shown to contain tubercle bacilli by guinea-pig injection, might reasonably be expected to result fatally within a short time.

It is of interest to note that in the present case, during the nine days after splenectomy, the red cell count remained high, between 8,800,000 immediately after operation to 7,400,000 on the day of his death, while the hemoglobin remained at over 120 per cent. This result one would expect if it is true that "the spleen is the graveyard of the red blood corpuscle" in the adult, although Pearce and Austin,²³ in a study of splenectomized animals, found results indicating the power of the lymph glands and liver cells to compensate, after the loss of the spleen, by taking up its function of destroying red corpuscles. However, Musser²⁴ found "that there was, after experimental splenectomy, a secondary anemia which lasted about two and one-half months." He also found a post-operative leukocytosis most marked twenty-four hours after operation, and lasting a variable time. His counts were continued one hundred and thirty-eight days in some cases, and the leukocytosis was still present. There was a marked increase in the poly-

²³ Jour. Exper. Med., December, 1912, vol. xiv.

²⁴ Archiv Int. Med., 1912, ix, 599.

nuclear cells, and a diminished lymphocyte count. In the present case this postoperative leukocytosis was a marked feature, reaching 87,000, with 98 per cent. of polynuclear cells on the second day after operation, and then gradually falling, but not back to normal.

It has previously been suggested that the tuberculosis of the spleen, in view of the autopsy findings, might be the simplest explanation for the polycythemia on the basis that the diseased spleen failed to destroy the red corpuscles. Other case reports of polycythemia, however, show numerous examples of the disease in which the spleen while enlarged was not tuberculous, and in twenty-six of the cases of tuberculosis of the spleen where the blood count was reported, collected by Winternitz, polycythemia was present only in six. Also, the condition of the bone-marrow in this and in other cases, and the blood-picture after splenectomy, would seem to indicate as a more logical presumption, that whatever may be its cause, the polycythemia, and in this case it was a polycythemia and not an erythrocythemia alone, had its direct pathological factor in the overproduction or overfunctionating of the bone-marrow. If this presumption is correct, then we can explain the enlargement of the spleen as an hypertrophy due to an effort to destroy the over-production of red cells. Finally, if there is a focus of tuberculosis elsewhere in the body from which the tubercle bacilli might enter the blood-stream, it would find in the spleen a place of diminished resistance. Thus, rather than as an etiological factor, the tuberculous spleen would be a result of the polycythemia.

Finally, while we may agree with Winternitz that in cases of tuberculosis of the spleen, when other tuberculous foci are not demonstrable, splenectomy may effect a cure; although our case proves nothing, it does add some evidence to the statement of Osler that splenectomy is contraindicated in erythrocythemia, and that when the two conditions coexist operative procedure can be of no value.

GIANT TUMORS OF THE CONUS AND CAUDA EQUINA.¹

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TUMORS of the cauda equina and of the conus cause symptoms which are considered fairly pathognomic. Nevertheless, the lesion

¹ Read at the meeting of the American Neurological Association, Washington, May 5, 1913.

is usually, at one time or another, mistaken for some other disease, and, on the other hand, patients are submitted to operation for tumor of the cauda or conus, and some other affection or no gross changes may be found. Then, again, the results of operation for tumor of this region, leaving aside the nature of the tumor, are by no means uniform. It is difficult for a neurologist to say to a patient with symptoms of cauda or conus tumor what will be the certain result of the operation advised. All this makes it imperative that the details of every case encountered should be published.

The tumors that we shall describe, probably originate from the pia over the roots or from the roots of the cauda equina themselves; they grow slowly, causing a few symptoms until they have attained a large size. Finally, when the symptoms are well-marked, the tumors fill the entire lower part of the spinal canal, surrounding the roots of the cauda equina and extending upward upon the conus and lumbosacral cord.

CASE I.—A male, aged forty-two years, Russian Hebrew, married, peddler. Complaints: Difficulty in walking, weakness and stiffness in the lower extremities. Pain in the centre of the small of the back radiating into the hips; inability to have full control of the vesical sphincter; irregular twitching of the right thigh, which always precedes expulsion of urine.

Duration of the symptoms was nine months, and the initial symptom pain, continuous, made worse by standing or walking, and relieved somewhat by lying down. Course of the disease steadily progressive. No history of syphilis.

On close inquiry, after the patient came into the hospital, an interesting story was obtained from him: which was that nine years before, while walking on a railway, he fell and struck his back. He was laid up for a fortnight. About one year afterward, that is, eight years before coming to us, he began to complain of pain in the lumbar region and in the posterior surface of the right thigh. This pain lasted for about eight or nine months, and he went to a hospital in New York City and stayed there for several weeks. Off and on since then he has had some pain in the back and in the thigh. Two years ago he had a severe attack and he justifies himself in stating that the beginning of his present illness was nine months before, by the fact that he was able to work until that time.

Physical Examination. Nutrition: No observable change. Motion: Station feeble, scarcely able to stand securely. Gait: jerky and spastic movement of the right foot in walking, the left normal. Paralysis: Right leg was weaker than the left. Mechanical restriction: No limitation of motion in the lower extremities. Marked rigidity of the lumbar spine. Reflexes: Right knee-jerk absent, left barely elicitable on reinforcement; both ankle-jerks absent; plantar jerks not elicitable; upper abdominals and epigastric reflexes lively; lower abdominals and cremasterics could not

be elicited; upper extremities normal. Disturbances of sensation illustrated by accompanying chart (Fig. 1); laboratory examinations were negative.

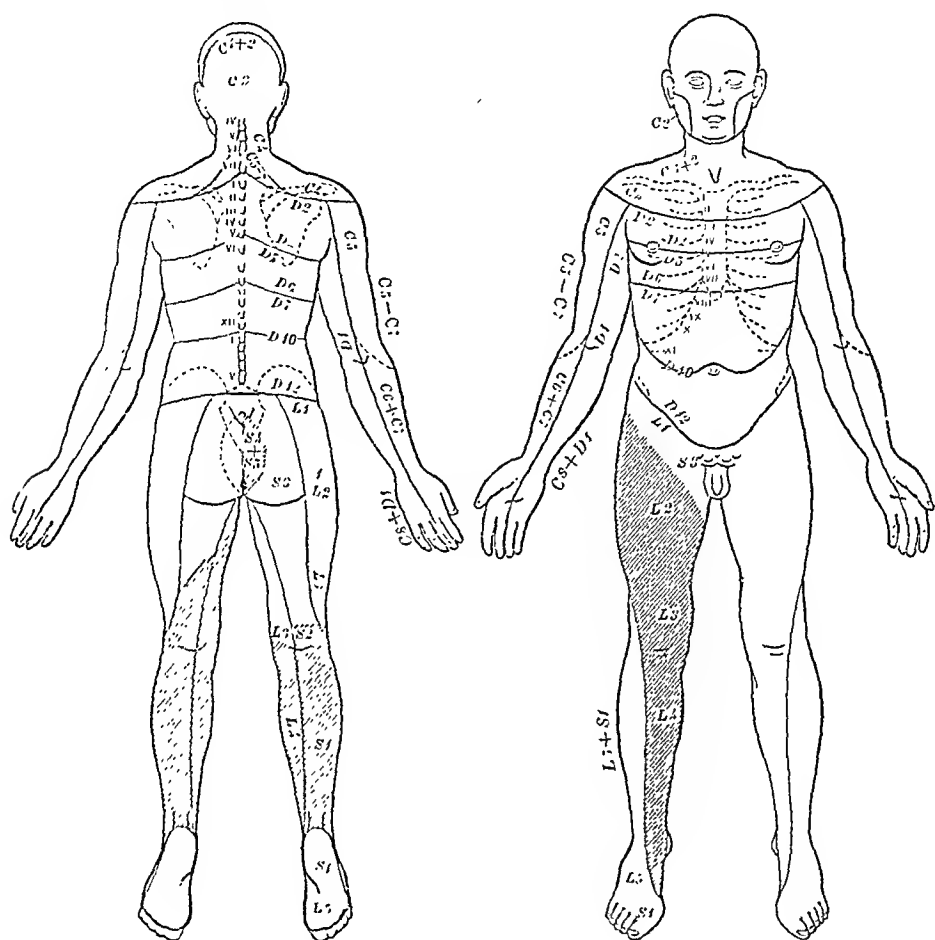


FIG. 1.—Case I. Nathan S., sensory disturbance for touch, pain, and temperature. Close shading, moderate diminution; coarse shading, very slight diminution in sensation.

Surgical History. January 27, 1910: Laminectomy (Dr. Elsberg). The spinous processes and laminae of the twelfth dorsal and first, second, and third lumbar vertebrae were removed. The exposed dura was of a bluish color on account of a tumor mass beneath it. After incision of the dura a large brownish growth (Fig. 2, I) was exposed, which enveloped the roots of the cauda equina and extended up on the conus. Above the tumor was well encapsulated and could be freed without difficulty; below it was impossible to separate it from several of the nerve roots without dividing them. The growth filled up the lower part of the spinal canal, and below, small fragments of tumor tissue were undoubtedly left behind. Suture of dura, muscles, fascia, and skin.

The tumor measured 2 by 5 cm., and weighed 14 grams; it was soft and not very vascular. It was an endothelial sarcoma. The

patient recovered from the operation, and the wound healed by primary union. After a few weeks he began to look badly, the urine became loaded with albumin, casts, and pus. Four weeks after the operation he was markedly anemic. On February 29, five weeks after the operation, he died in a convulsive attack. No autopsy permitted.

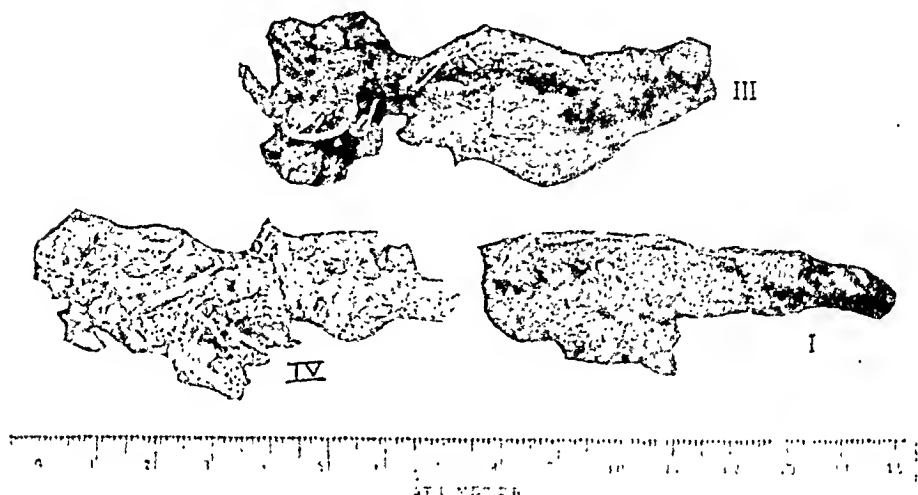


FIG. 2.—Giant tumor of the cauda equina removed at operation.

CASE II.—Woman, Russian Hebrew, aged twenty-five years; married. Complaints: Pain in the back radiating down the legs, more severe in the left than in the right leg; weakness in the lower extremities; difficulty in passing urine. Duration of symptoms had been about two and a half years, initial symptom being the pain. This pain began about a fortnight after she married, gradually increased in severity, and since the birth of a child, ten months after marriage, it had grown worse rapidly. Pain increased by any attempt at movement, such as walking or going up and down stairs, and was least when lying down.

She had been subjected to many kinds of treatment. Had worn arches for double flat-foot; had been in a plaster jacket for alleged spinal trouble, etc.

Physical Examination. Nutrition: Nothing noteworthy save a faint systolic murmur at the apex, hemie in character. Station: Weak and uncertain. Gait: Shuffling, "rooster" gait. Paralysis: Drop-foot on both sides. Marked stiffness of the lumbar spine. Reflexes: Knee-jerks faintly elicitable; ankle-jerks present; plantar flexion; abdominal and epigastric reflexes present. Sensation: As indicated on the chart (Fig. 3).

It is noteworthy that percussion on top of the head caused intense pain in the lumbar spine, and that the lumbar vertebrae themselves were tender on percussion.

Laboratory examinations were all negative, save that the lumbar puncture brought forth a dark yellow fluid which contained no cells, gave a negative Wassermann, and coagulated solid on application of heat.

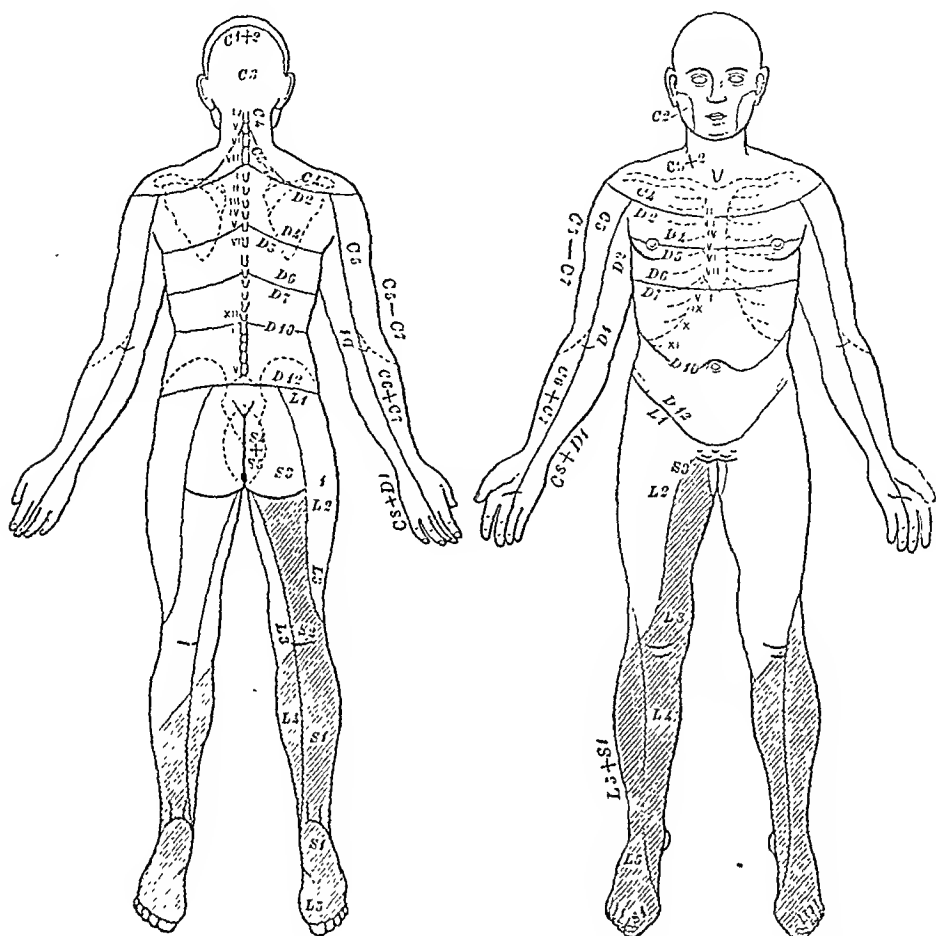


FIG. 3.—Case II. Mrs. P., very slight disturbance of touch, pain, and temperature over shaded areas.

Surgical History. December 3, 1910: Laminectomy (Dr. Elsberg). Removal of spinous processes and laminae of the third, fourth, and fifth lumbar vertebrae, later of the second and first lumbar and the twelfth and eleventh dorsal vertebrae. The exposed dura was of a bluish color, and did not pulsate. There was evidently a large neoplasm within the dural sac. The dura was incised, exposing a large reddish-brown tumor mass, which surrounded the roots of the cauda equina and filled up the entire spinal canal to the lowermost part exposed. Above it was necessary to remove the eleventh and twelfth dorsal and first and second lumbar arches, and to incise the dura upward, before the upper end of the tumor was exposed. The growth extended upward upon the conus and lumbosacral cord, and was well-limited and but slightly adherent

to the cord. During the various manipulations the tumor gradually bulged out of the canal until it seemed about three times as thick as when first exposed. Below could be seen some roots of the cauda equina surrounded by tumor tissue. It was deemed advisable to delay the removal of the growth in order to allow the tumor to be extruded from the canal. The wound was therefore closed without drainage.

December 10. The wound was reopened and the tumor was found markedly extruded. With little difficulty the growth was freed from the conus and from the inner surface of the dura, which was everywhere smooth and glistening. The growth was likewise easily freed from the roots of the cauda, although it was firmly adherent to the filum terminale. Several fragments of tumor tissue had to be separately removed with a sharp spoon. The wound was closed in the usual manner.

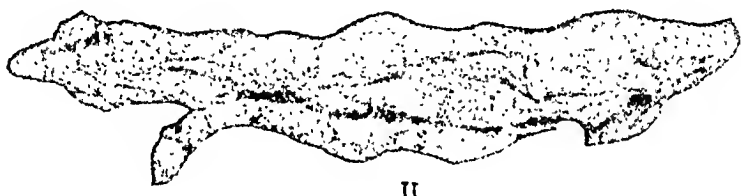


FIG. 4.—Giant tumor of the cauda equina and conus removed from Mrs. P.

The tumor removed (Fig. 4) measured 14 cm. in length and 6 cm. in circumference in its widest part, and was reported by the pathologist as endothelial sarcoma. Convalescence from operation uncomplicated.

December 17. Slight flexion and extension at the knees was possible.

January 6, 1911. Power in the right lower extremity was better than in the left, flexion at thigh and hip—about 75 per cent. of the normal on the right, about 30 per cent. of the normal on the left.

January 20: Discharged from the hospital. Patient had gained much flesh and strength; could stand on her feet when aided; was able to extend and flex both legs with ease; knee- and ankle-jerks were still absent.

September 6: Patient continued to gain flesh and strength. Could walk, but had trouble on account of the persistent foot-drop. Knee- and ankle-jerks were still absent. Patient was free from pain; no disturbance of sensation could be found.

CASE III.—Male, Russian Hebrew, aged thirty years, married, painter. Complaints: Pain starting in the middle of the small of the back and extending down both thighs and legs; weakness of the lower extremities so that walking was difficult; inability to pass urine; impotence.

The initial symptom was pain in the middle of the back, which was not continuous in the beginning. It was made worse by exercise, and was relieved by hot applications and a hot bath. His first incapacity was in bending over and in straightening up after he bent over. After the pain had existed in one lower extremity for about three months it appeared in the other. At this time he was seen by a number of neurologists and was treated as a case of sciatica. His symptoms had been in existence for about two years when we first saw him. Course of symptoms had been steadily progressive.

Physical Examination. Nutrition: The skin of the feet was soft and shiny, the nails strikingly convex, with transverse markings. Motion: When the feet were lifted from the ground there was distinct drop-foot on both sides. Gait: Typical "rooster" gait. Station: He stood fairly securely when his feet were together when the eyes were open, but swayed when the eyes were closed.

There was no muscular atrophy. Reflexes: knee- and ankle-jerks absent. Plantar reflex was flexor in type; abdominal and epigastric reflexes were lively; cremasteric reflexes could not be elicited. There was a diminished response to the faradic current in the peroneal muscles, more marked on the right side. There was distinct stiffness in the lumbar vertebral column, and the lower lumbar spines were sensitive to pressure and percussion. The sensory disturbances are indicated in Fig. 5. There was a distinct area of exquisite hyperesthesia at the upper border of the sacrum. On doing a lumbar puncture, the needle, after entering the cavity, gave the operator's hand a sensation of there being some friable substance encountered, and the patient complained of a burning sensation transmitted down the right hip and leg. No fluid was obtained.

Surgical History. October 4, 1911. Laminectomy (Dr. Elsberg). Removal of the spines and laminae of the first, second, third, and fourth lumbar vertebrae and later of the eleventh and twelfth dorsal. Shining through the dura, which was very thin, was a reddish-brown tumor mass, over which were spread the roots of the cauda. Incision of the dura revealed a large tumor, which filled the spinal canal from the sacrum below to the conus above. The actual removal of the growth was left to a later stage, so as to allow of the extrusion of the growth.

The tumor was removed one week later; above, it was well limited and easily freed from the conus; below it surrounded the roots of the cauda and not all of the tumor could be removed. In spite of

careful dissection, small fragments of tumor tissue had to be left behind. Bleeding was moderate; closure of the wound in the usual manner.

The tumor was 10 cm. long (Fig. 2, III), and was reported as being an endothelioma.

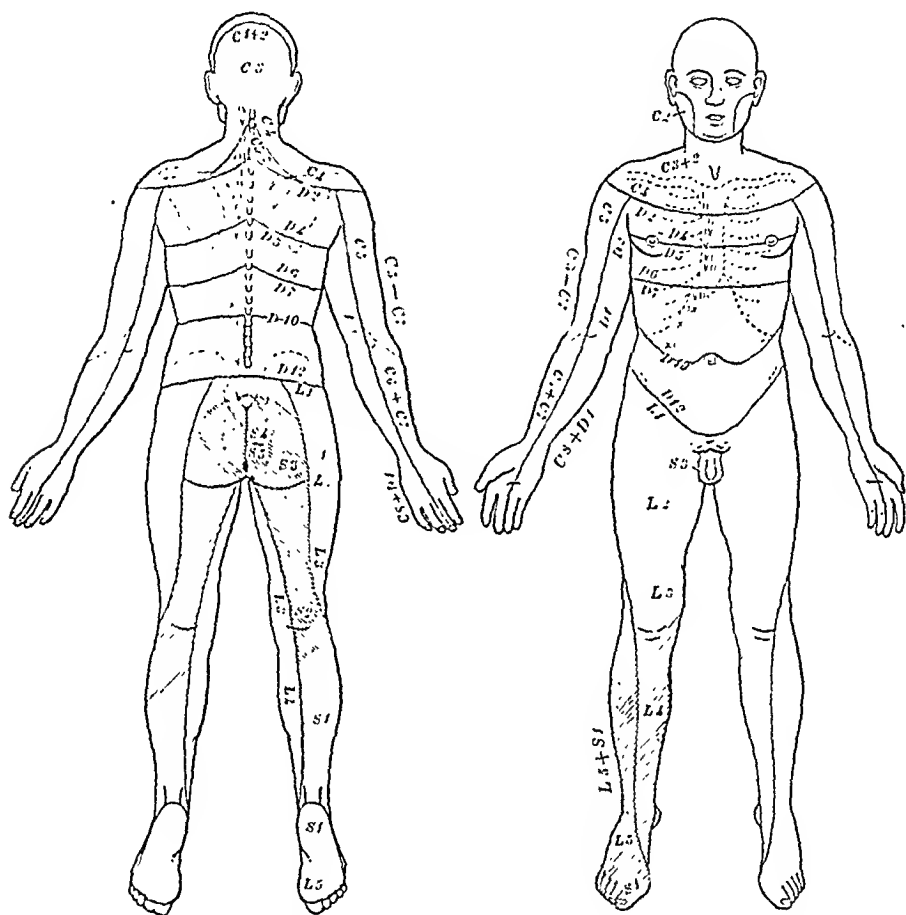


FIG. 5.—Case III. J. S., sensory disturbances for touch, pain, and temperature. (Shading the same as in Case I.)

Convalescence was uneventful. Two weeks after the operation the patient was able to urinate voluntarily, and the pain in his back and limbs was somewhat less. He was discharged from the hospital three weeks after the operation. Two months later, sexual power had returned, but the patient complained much of a stiff feeling in his legs and of frequency of urination.

March 1, Patient had been receiving injections of Coley's fluid and x-ray treatment twice each week. Still complained of stiffness in his legs and frequency of urination; knee- and ankle-jerks were still absent. No longer had foot-drop; sensory disturbance unchanged.

January 22, 1912. The patient was last examined on this date. His complaints were: Pain in the back and right thigh; feeling of stiffness; obstinate constipation; no feeling when his bowels moved; weakness of the legs; incontinence of urine.

He stood securely, with his back not stiff, walked with a stick, with a slightly shuffling gait. The tendon-jerks of the lower extremities were absent, and the only striking difference from his condition before the operation was in the objective sensory disturbance and the disappearances of the foot-drop.

Each of these three patients presented a clinical picture and physical signs so similar to the others that a diagnosis of the similar nature of the disease could be made. In Case I the diagnosis was suspected; in the two succeeding patients the diagnosis of giant tumor of the cauda equina endothelioma or endothelial sarcoma was made before the operative interference.²

The important features of the clinical histories in our patients were the following:

1. A history of two or more years' duration.
2. Pain in the small of the back, sooner or later extending down one and then the other extremity.
3. Stiffness of the back in the lumbar region.
4. Increasing stiffness and weakness of the lower extremities, with loss of power of dorsal flexion of the foot.
5. Slight disturbances of the bladder and rectum.
6. The patients were treated for sciatica for long periods.

The important features of the clinical examination were the following:

1. Rigidity of the lumbar vertebral column.
2. Weakness and stiffness of the lower limbs.
3. Paralysis of the peroneal groups of muscles and sometimes of the tibialis anticus group.
4. Drop-foot on one or both sides.
5. Absence of knee- and ankle-jerks.
6. Tenderness of the lower lumbar spines.
7. Irregular and unsymmetrical sensory disturbances.
8. Lumbar puncture was negative, or yellow fluid which was not cerebrospinal fluid was withdrawn.
9. Wassermann test and x-ray negative.

The typical findings at operation consisted of a large reddish-brown, not vascular, tumor within the dura, which filled up the entire lower part of the spinal canal, surrounded the roots of the cauda equina, and extended upward on to the conus, with which it was not closely connected. The growth was not intimately connected with the inner surface of the dura, and could be easily freed

² One of us has operated upon two additional patients. One patient was on the service of Dr. Bailey at the Neurological Institute, the other was a private patient referred by Dr. W. M. Lesnysky, of New York.

from it, after which the inner surface of the *dura mater* was found to be smooth and glistening. The growths were well encapsulated above, but were closely connected with the nerve roots below.

The typical history and findings in these patients were similar to the so-called syndrome of epiconus lesions described by Minor of Moscow, which may be outlined as follows: The patient begins to complain of pain and stiffness in the back, extending down the posterior aspect of one and then of the other thigh. The pain is intermittent at first, later it is continuous. After the expiration of one year or more the symptoms become worse, one or double drop-foot appears, the lower limbs become weaker and stiffer, and knee- and ankle-jerks disappear. Then follow difficulties in the functions of the bladder and rectum, irregular sensory loss, rigidity of the lumbar vertebral column, and tenderness of the lumbar spines. Peroneal palsies are regularly found, with electrical changes. By lumbar puncture no fluid is obtained, because the entire lower part of the spinal canal is filled by the tumor mass, although yellow fluid in small quantity may be withdrawn from the tumor. The patients are often suspected of tabes, and usually have been treated for long periods for sciatica.

PECULIAR FEATURES OF THE TUMORS, AND REMARKS. We are fully cognizant of the fact that, in a general way, the symptoms and signs we have outlined are those generally described as characteristic of lesions of the cauda equina and conus. But they have been combined in a peculiarly characteristic manner in our cases.

The late appearance of bladder and rectal disturbances in the patients lends support to the view of Spiller³ and of van Gehuchten as against that of Müller⁴ that bladder and rectal symptoms need not appear early in intradural pressure upon the roots of the cauda equina.

Another peculiar feature in these patients was the relatively small evidence of sensory disturbances. According to some authors (Laquer, Kummel Schmolli), sensory symptoms, in lesions of the cauda equina and conus, may be absent for years. Müller claims that in the lower end of the cord the sensory roots are larger than the motor roots, but he agrees with Klineberger that the sensory elements have a marked resisting power. It is difficult to understand why there is not a greater sensory loss in these patients, with large tumors which fill up the entire lower part of the spinal canal. The typical anesthesia in the perineum, genitals, and around the anus was usually incomplete, ill-marked, or absent. This was the more surprising as at operation the tumor was usually found to surround the roots of the cauda—those centrally situated as well as those on the outside. That these large tumors were under con-

³ AMER. JOUR. MED. SCI., 1908, xxxv, 368.

⁴ Deutsch. Zeit. f. Nervenheilkunde, 1899, xiv

siderable pressure was proved by the fact that as soon as the dura was opened they bulged markedly out of the canal.

The tumors were relatively benign in their course, they had no tendency to perforate the dura or to invade the surrounding bony structures. In this respect they differed from many of the cases of diffuse intradural sarcoma in the literature (Schultze,⁵ Spiller,⁶ etc.) and were like those reported by Selberg⁷, Warrington,⁸ Klineberger,⁹ etc.

The results of the operative interference were not satisfactory, although there was considerable improvement in two of our patients. It was impossible to remove the growths entirely, although most of it could be removed if the operation be divided into two stages so that the tumor be allowed to extrude from the spinal canal in the manner described. In the one patient who received injections of Coley's fluid and x-ray treatment, not much was gained thereby. While the danger from the operative interference was small, our only hope for radical removal lay in our ability to recognize the existence of the tumor early and to refer the patient to the surgeon early. If the patients had been operated upon before the tumors had attained such large size, radical removal might have been possible.

SOME CASES OF HYPOTENSION ASSOCIATED WITH A DEFINITE SYMPTOMATOLOGY.

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It is difficult to state just how low the systolic pressure may fall and yet be considered normal. In an individual who has been observed over a period of time and in whom one has determined a uniform pressure, any deviation from this standard may with justification be regarded as abnormal if not pathological. But for the rank and file of individuals it must remain a purely arbitrary judgment at what figure to place the lower limit of normal pressure, and the standard thus erected must be regarded as but an individual opinion, nothing more.

Janeway draws the line between normal and subnormal systolic pressure at 100 mm. Hg. (R.R. 5 cm.) and 90 mm. (12 cm., G.).

¹ Mittheil. a. d. Grenzgebieten, 1903.

² Beiträge z. klin. Chir., 1904, xliii, 197.

³ Monatsschr. f. Psych. u. Neurol., 1908.

⁵ AMER. JOUR. MED. SCI., 1908, cxxxv.

⁶ Lancet, 1905, ii, 749.

I prefer using the auscultatory method, to place the limit at 120 mm. Hg., and I believe pressures below this must fall in the category of lowered or low blood pressure. Such a limit is purely empirical, and observations made with a standard instrument, with a uniform method, and under uniform conditions, in many thousands of healthy individuals, this procedure alone can fix the limit with any degree of accuracy.

The maintenance of blood pressure depends primarily on the preservation of the normal peripheral resistance and on the force of the cardiac systole. The following lines copied, in the main, verbatim from Cannon¹ gives a concise view of conditions which tend by decreasing peripheral resistance, to cause lowered blood pressure.

"Fall of pressure is seen in poisoning by chloral and alcohol, both of which paralyze the vasoconstrictor centre. The collapse of the circulation that sometimes occurs in the course of certain of the infectious diseases, such as pneumonia and diphtheria, may be in part due to this cause. In surgical shock, again, the widespread abolition of vascular tone is accomplished by a low blood pressure. In these instances the reduction may be due to a rapid pouring of the blood out of the relaxed vessels or to a stagnation of the blood in the veins to such an extent that the heart does not receive a sufficient supply to continue its normal discharge. Which of these conditions plays the more important role is not yet determined. Henderson has argued from evidence which he has accumulated that the condition of shock² is attributable entirely to a failure of the supply of venous blood to the heart.

"As is well known, vasoconstrictor tone can be diminished at will by use of the nitrites. A few whiffs of amyl nitrite produce a sharp drop in arterial pressure, which is, however, soon regained.

"A physiological condition attended by lowered arterial pressure is sleep.

"A low pressure may be due not to vasodilatation but to a weak heart, and any agency used to increase vasoconstrictor tone under these circumstances is likely to stop the heart at once. Indeed, my attention," says Cannon, "has recently been called to a case of precisely this character in which the administration of adrenalin to raise the pressure was followed by instant death—the laboring heart was overburdened by the sudden increase of load and stopped immediately. Until the part played by each of the two factors, therefore, the heart and the arterioles, is clearly discriminated the intelligent treatment of any disturbance of normal arterial pressure is impossible."

¹ Boston Med. and Surg. Jour., 1911, clxv, 672.

² Amer. Jour. Phys., 1910, xxvii, 158.

The causes of hypotension or the condition in which hypotension is a phenomenon may be classed as follows:

1. Acute infections, excepting epidemic cerebrospinal meningitis.
2. Chronic wasting diseases: carcinoma, tuberculosis, cachexia from whatever cause, Addison's disease.
3. Hemorrhage, drugs, chloroform.
4. Nervous diseases: general paralysis of the insane neurasthenia, after epileptic seizures, sometimes in tabetic crises, after lumbar puncture, Basedow's disease (at times), osteoarthritis, exhaustion, shock—surgical or anaphylactic.
5. Cardiovascular diseases: tachycardia, dilatation of the heart, arteriosclerosis (at times), mitral stenosis, decompensatory cardiac lesions.
6. Blood dyscrasias: anemia, polycythemia cum splenomegaly.
7. Renal condition: cyclic albuminuria, nephritis (at times) amyloid disease.
8. Intoxications: alcohol, tobacco, acute adrenal insufficiency.
9. Terminal hypotension preceding death.

A search of the literature reveals a lamentable paucity of specific articles on low blood pressure, the subject of hypertension apparently having dominated the interest and riveted the attention of writers. Anyone who includes blood-pressure estimations in the routine examination of every patient must have been impressed, however, with the not infrequent occurrence of blood pressures below 120 mm. Hg., blood pressures lying between 110 and 120 mm. Hg. Less common are the pressures lying between 100 and 110 mm., and still more rare are those between 80 and 100 mm.; but apart from exciting surprise at the abnormally low tension the phenomenon seems to have been little investigated. It is on account of the very cavalier treatment of the subject, that contributions devoted to its explanation or papers dedicated to report of cases are extremely valuable. If one reads all references to hypertension he will be astonished at the amount of research performed along these lines, and will gather the incorrect and hasty impression that hypertension is the only problem in sphygmomanometry. It cannot be denied that a persistent high blood pressure carries in its train more destruction and more pernicious damage, and that therefore it deserves more consideration than does low pressure; yet this seems hardly a satisfactory explanation on for the neglect which hypotension has experienced.

Its importance and significance in certain surgical conditions, notably shock; in certain clinical crises, such as anaphylactic shock; and its almost constant presence in acute fevers or infections; these are well-established facts. They are valuable additions to our knowledge, no doubt, but hypotension in cases other than in the above, in individuals who present no apparent lesion but who con-

sult the physician about symptoms to which the specious diagnosis neurasthenia might be too readily applied, hypotension in these patients is a subject well worth the study. Whether the low blood pressure in certain persons is a cause of the symptoms or whether it is a result of some agent causing the symptoms one cannot say.

The subject of hypotension has made a special appeal to Münzer,³ who presents his paper with three prefatory remarks, with the censure that the subject has received but scant attention, with the expressed aim to separate certain cases into groups, and with the frank admission "wobei ich mir dessen (einige Formen) wohl bewusst bin, dass es bei dem gegenwärtigen Stand unseres Wissens nicht möglich ist, das Gebiet systematisch zu erschöpfen." Münzer endeavors to classify his cases in groups, and succeeds in forming six. Some of his arguments for this grouping and the basis for his diagnosis seem to be dogmatic rather than irrefutably sound. His paper, nevertheless, has this value, that it frankly invites criticism, its avowed object being to stimulate interest in the subject of hypotension.

The first of Münzer's groups is the hypotension seen in arteriosclerosis. He believes that this is a common cause of low pressure, and offers as explanation that the blood flows through the large hard vessels, as does a fluid through an unyielding tube; there being no periodic distention of the vessel wall, the tension is lowered. In some instances the pressure was as low as 85 systolic, 75 diastolic. A common trilogy of symptoms was headache, vertigo, and even fainting.

A second group of cases occurs in what Münzer believes to be status thymo lymphaticus. Wiesel⁴ and later Hedinger⁵ observed hypoplasia of the chromaffin system in cases of this kind, and since Sehur and Wiesel⁶ have demonstrated hypertrophy of the chromaffin system in cases of hypertension, Münzer believes one may, by analogy, expect hypoplasia to be associated with low blood pressure. He proceeds on insufficient grounds, I believe, to arrange certain cases in the category of status thymo lymphaticus.

The remaining groups of disease associated with hypotension are orthostatic albuminuria, chronic nephritis, paroxysmal tachycardia, and cachectic conditions.

That hypotension is by no means an uncommon feature of arteriosclerosis there can be little doubt, as Huchard's reference in the *Transactions of the XVI International Medical Congress*, in Budapest (1909), will show: I have under my care at the University Hospital Medical Dispensary a case in point.

³ Wien. klin. Woch., 1910, p. 1341.

⁴ Virchow's Archiv, 1904, Band cxxvi.

⁶ Deutsch. med. Woch., 1907, No. 51.

⁵ Ztsch. f. Pathol., 1907, p. 527.

Thomas MacR., aged sixty-seven years, engineer, was referred from the eye dispensary with retinal hemorrhages in the left eye. There was decided arteriosclerosis and urinary findings suggesting interstitial nephritis, *i. e.*, polyuria, low specific gravity, albumin, and casts. The blood pressure, which in this case was a variable quantity, had been as low as 123 to 80 mm. Hg.

I have been most interested in cases of low blood pressure occurring in the absence of any demonstrable organic lesion. These have been patients, for the greater part, on the ascent or the crest of the curve of life, who have presented certain symptoms common to each, and who have been markedly improved by practically the same therapeutic measures. As illustrative cases, the following are quoted. (Auscultatory method; Stanton sphygmomanometer; Widecuff.)

CASE I.—H. F., female, aged twenty-three years, consulted me July 14, 1911, on account of headache. Patient had been complaining of headaches for the previous two or three years. The attacks were intermittent, there being often two or three months' interval, and then again repeated several times in the same week. The headaches were situated in the top of the head and were described as pulsating and throbbing in character, with a feeling of tenseness. The patient could ascribe no cause for the headaches, although sleep usually brought relief. She had less endurance than formerly, and "played out" readily. Bowels were regular, no gastric symptoms. Eyes were thoroughly refracted five years before.

The family history and previous medical history were negative. The menses were regular, but the patient had some pain in the right iliac region, from which she suffered a good deal at irregular intervals. There was no aggravation of headache at these times nor at the time of menstruation.

The physical examination was negative. The blood pressure at the time of the first visit was 80-55 mm. Hg. Under treatment during the next four months the blood pressure rose to 120 mm. Hg., and with this improvement the headaches disappeared almost entirely.

CASE II.—E. C. W., female, aged thirty years. Referred by Dr. Langdon. On the evening of September 25, 1911, I was summoned to give relief for a severe headache. The patient stated that since the spring of 1911 she had suffered intensely with violent frontal headache, vertigo, swelling of eyes and of ankles, scanty urine, and less endurance. In August, 1911, she underwent a severe nervous strain, and admitted in September that she was at the "end of her rope."

Patient says she has at times of periods pain over the right ovary, and that her menstruations are irregular. Owing to the fact that

her mother experienced the menopause when thirty-five years and her maternal grandmother had "change of life" at thirty-two years, patient is apprehensive and fearful that her present symptoms may be phenomena incidental to what seems to be a familial early menopause. Bowels regular.

On examination the urine was found to be negative. The blood: Hemoglobin, 80 per cent.; erythrocytes, 4,030,000; blood pressure 110-75. Large doses of bromides brought about amelioration from the headaches, and the patient was sent to the country for a three weeks' stay. On her return she stated that in this time she had had four severe attacks. Blood pressure, 115-65; hemoglobin, 90 per cent.

In December, at which time the blood pressure had risen to 120-70, the patient stated that she had not felt so well for years, and that she had not had a headache for over a month.

February 28, 1912, patient came to see me on account of slight return of headaches during the previous week. Blood pressure, 110-60 mm. Hg.

March 20, 1912, with a rise in pressure, there was subjective improvement, and apart from a feeling of distention after meals the patient felt "first-rate."

CASE III.—F. J. G., male, aged fifty-one years, lawyer. Referred by Dr. E. I. Keffer, November 28, 1911. His chief complaint was failing of memory. Patient had been for thirty years of a nervous disposition, and had received sporadic treatment during this time for his trouble. Lately he had found his memory to be less keen in court work; he was so fearful of himself in public that he was beginning to devote himself entirely to office consultations. With the failing memory he had had persistent insomnia, and was subject to unaccountable attacks of irritability. He complained of no headache, but described his mental symptoms as if a cloud were enveloping his brain. Vertigo persistent, but not severe, was an unpleasant symptom. He "played out" both mentally and physically; would get up tired in the morning, and had difficulty in concentrating his attention. He was insistent that he had not worked hard for five years, but his law partner adduced evidence to the contrary.

The patient had some gastric symptoms, flatulence, belching, and acid eructations. Appetite was variable, but ate everything. Bowels were regular. Apart from overindulgence in tobacco there was nothing in the patient's further history which seemed to have a bearing on the case.

On examination his lungs were negative; heart was enlarged, slightly to the left; there was a systolic murmur at the apex transmitted slightly. After removal of a test meal (125 c.e., total acid 74, free HCl 32) the stomach was found to be slightly dilated,

lower border 2 cm. below umbilicus. The liver was slightly palpable. Blood: hemoglobin, 90 per cent. Urine and feces negative; blood pressure, 105-55. Eyes were refracted five years before.

Treatment seemed to be ineffective with this patient, that is, blood pressure rose to 116, but could be brought no higher. The patient had persisted, however, with the suggestions made to him and at the last visit, September 23, 1912, stated that he saw a marked improvement since a year before, and that for the last two weeks he had felt better than ever before. Blood pressure at that time was 123-55. He had regained his confidence when talking in public and had lost his fear of being unable to express himself in the courts.

CASE IV.—R. E. G., male, aged twenty-one years, statistician. Referred by Dr. Knowles Feb. 15, 1913. Chief complaint, constipation and eruption on the face. Dizziness from "some cause or other."

The acne he had had for five years, but constipation made its appearance five or six weeks before. The previous summer he began to have dizzy spells, which were gradual in onset. These attacks followed exercise or any mental stimulus. Although he does not faint, he seats himself as quickly as he can, as he thinks he might fall if he stood. There is no nausea or vomiting. He feels perfectly well as soon as the dizziness passes off, which it does in a few minutes. He has no headaches. Eyes were examined October, 1912.

Patient takes a good deal of exercise in the form of walking, although he studies, as a rule, about ten hours a day. No gastric symptoms. He is losing weight; best weight 130 pounds, three years ago; now 117 pounds.

Patient's habits are exemplary. The family history discloses a nervous taint in all members of the family.

Examination is negative. Blood pressure, 110-60.

March 22, 1913. No more dizziness. Bowels regular; weight 121½ pounds; blood pressure, 120-60; feels fine.

CASE V.—G. L., male, aged forty-two years, laborer. Admitted to my dispensary at the University Hospital January 20, 1913, complaining of intermittent spells of dizziness.

Patient states that these spells come on once every week or two. Each attack was preceded by a feeling of warmth, then his sight was blurred. There was numbness in the head, followed by vertigo. Patient reels if standing, and has to support himself to avoid falling. "Spells" only come on while standing. If patient lies down the spell passes off in about an hour, but if he remains standing they may last half a day. As he recovers, he is nauseated, has a gnawing pain in the epigastrium, and sometimes vomits.

He is unable to talk "much." No symptoms remain after the spell. He is constipated, and takes laxatives several nights a week; otherwise the gastrointestinal tract is negative.

During the attacks he has a bearing-down sensation of the brows and double vision. He notices sensation of constriction in fauces and pharynx. Mouth floods with saliva, and at the same time he experiences difficulty in swallowing. This is followed by a feeling of nausea, and at times he may vomit. He also feels an epigastric pulsation. He has difficulty in breathing, his head feels too heavy for his body, and he dreads falling from dizziness, therefore keeps his eyes on the ground during attacks. He has no noises in ears. Had eyes refracted about a year ago and lenses corrected. Hypermetropic astigmatism, but this has in no way influenced his attacks, which come with some degree of periodicity once every week. Has some slight palpitation of heart on exertion; marked hypotension.

These five serve as illustrations of certain phenomena associated with hypotension. Although not each symptom is present in every instance, the chief symptoms in these cases are headache, vertigo, mental and physical tired. These symptoms have been significant, inasmuch as one or all have been the chief complaint of the patient, and with rise in pressure the patients have been much improved. The question which naturally arises is, What is the etiological factor?, and to this there must be a confession of ignorance. Tuberculosis must be the condition to suspect whenever there is a lowered blood pressure, provided no other cause such as tabulated above can be found, but in none of these five patients whose histories have been reproduced was there slightest evidence of this infection. It would be purely supposititious to hold that a small lesion might still be present and escape careful physical examination. There is no clinical evidence to support this hypothesis, and improvement followed a course of treatment which would presumably have had a somewhat opposite effect in tuberculosis.

Can the low pressure be an expression of auto-intoxication? Inasmuch as this theme has been so well worn that we perceive the insubstantial warp, one should omit it from his medical diagnosticon. The more closely one studies the cases of supposed auto-intoxication the more frequently does he find an underlying organic condition to explain the symptoms, such as hepatic cirrhosis, enteritis, redundant sigmoid, visceroptosis, etc. If one is to take the symptomatology as given by Combe ("Auto-intoxication intestinale") as an indication of an underlying intestinal intoxication, he will be able to ascribe to the latter practically every symptom flesh is heir to. There may be *bona fide* cases of auto-intoxication, but these must be very few. At any rate the methods at our disposal for their recognition are at fault, and an estimate formed from quantitative and qualitative urinary examinations, no matter how

painstaking and exact, is by no means a correct one. Feeling that auto-intoxication is a poor diagnostic term I prefer not to consider it as a cause or as the cause of the symptoms exhibited by these patients.

Were constipation a common feature in these cases it might be assumed that retention of feces with absorption of waste products—in other words, auto-intoxication again—might be the cause of the hypotension. Correction of the constipation then might bring about amelioration of symptoms. In only one case was constipation a feature, and as no drugs were given for this, reliance being placed on certain exercises, the problem is not so simple. It is a question, moreover, whether constipation alone is associated with absorption of certain waste products. I am by no means convinced that it is. Again, it is a nice point to decide whether constipation is the cause of the hypotension or whether the hypotension, with its other symptoms of tire, might not bring about relaxation of the intestinal musculature as it does of the voluntary muscles. And may it not be true that with increased vasomotor tone, normal action of the intestines has been brought about, rather than that relief from constipation has raised the blood pressure by eliminating the absorption of waste products?

The diagnosis of neurasthenia applies here as little as does that of auto-intoxication. Neurasthenia seems to be a convenient diagnostic catch-all for conditions not perfectly understood, and great care should be executed in making this diagnosis. Moreover the blood pressure is not lowered in neurasthenic states, but raised, as shown by Stursberg⁷ and Stursberg and Schmidt.⁸

I confess that I can offer no explanation of the hypotension. The significant features in these cases is that subjectively they were alike, and with the same method of treatment all showed improvement and some were cured, and with this improvement as cause or effect, was associated an increase of blood pressure.

TREATMENT. The treatment which has been given these patients consists essentially of the following: They are instructed to go to bed at a reasonable hour and to rise at a certain time each morning. Immediately on rising they are to perform a series of exercises, consisting of free movements, somewhat after the following plan:

1. Stand erect with the arms extended and the fingers in contact above the head. Stoop forward and try to touch the floor with the finger-tips, moving slowly, and return again to the original position.

2. Lie at full length on the floor or bed upon the back, with the

⁷ Deutsch. Archiv. f. klin. Med., 1907, xc, 548.

⁸ Münch. med. Woch., 1913, p. 174.

hands under the hips, and bring each leg alternately and slowly to a position at right angles to the body. Perform the same motions with both legs conjointly.

3. Lying at full length upon the back, the hands clasped behind the head, bring the elbows in, bend the body forward until the face touches the knees, returning again slowly to the original position.

4. Standing position: extend the arms sidewise, the elbows straight, until the hands meet above the head. Stretch the arms as much as possible in doing this. Inhale deeply as the arms go up, and exhale slowly as they come down.

5. With the hands on the hips, the thumbs behind, without moving the feet, turn the trunk as far as possible to the right, then to the left. As the body turns rub the fingers deeply into the abdomen.

6. Raise the arms laterally, the palms upward, until the level of the shoulders is reached, bring them forward until the fingers touch; then reverse the movement, extending the arms backward as far as possible, at the same time rising upon the toes.

7. Breathing: Hands at hips, head backward bend, inhale through nose; head erect, exhale through nose and mouth five to ten times.

In order that the exercises should have the desired effect, they must be performed regularly, every morning, at least ten minutes being devoted to the task. They should at first be performed slowly, with intermissions of a few seconds for rest and deep breathing. As the muscles become accustomed to the work they may be increased in rapidity and duration, but never to the extent of producing exhaustion or prolonged breathlessness.

Following these or some such exercises, a shower-bath, first hot and then as cold as can be well borne, should be taken, but if there are no such appointments, a good modification can be obtained from the following:

Stand erect in the tub in which a little hot water remains, and sponge the entire body quickly with cold fresh or salt water; or pour a pitcher of cold water over the back and spine, or use a douche or spray. This should be immediately followed by a brisk rub with a coarse towel, continued long enough to produce redness of the skin. Following this, rest in the recumbent position, well covered up, for five or ten minutes before dressing. Bathroom should be warm.

Definite rules are given for the number of hours work to be done a day, and a certain amount of relaxation is insisted upon. Golf, horseback-riding, tennis, walks in the country, are all useful in bringing about a temporary dropping of business, professional, or domestic trials.

In all of these cases I have prescribed ascending doses of tincture

of nux vomica, beginning with 15 drops three times a day after meals and increasing 3 drops a day, so that the first day, 15 drops three times a day are taken, then 16, 17, and so on. The limit to the increase is the first sign of the physiologic action of the drug, and when this is obtained the dose is dropped 5 drops and maintained there for a period of two to five days, after which the number of drops is decreased 15 drops a day, dropping from 45, for example, 40, three times a day, to 35, three times a day, etc. The decrease is continued to the original 15 drops three times a day, which dose is maintained for a week, and then the nux vomica is discontinued.

Regarding the dose of nux vomica which may be given, patient Case III took 75 drops three times a day without experiencing any physiologic effect of the drug. The individual tolerance to strychnine is variable, and not everyone can take such large doses without feeling some toxic effect.

For the coexisting constipation use was made in the following manner of the exercises described by Fernet.⁹ I quote from my article in *Progressive Medicine*, December, 1912, p. 102.

"The patient, before arising in the morning, is to lie on the back, and take five or six deep breaths, with the mouth closed, protruding and retracting the abdomen with each respiration. After a few moments of natural breathing the same procedure is repeated, and is kept up for five or six times. By means of the deep breaths, Fernet claims that the abdominal organs are subjected to a kind of massage, which is further augmented by manual massage during the remissions of normal breathing. After rising and bathing the patient should partake slowly of breakfast, and afterward go to the toilet, whether he feels the desire to defecate or not. If there is no bowel movement the breathing exercises should be repeated, and in place of the massage, rectal gymnastics should be practised, consisting of voluntary movements of the anus, efforts of expulsion and of retension. Under no condition should there be any straining."

Excessive indulgence in tobacco, alcohol, tea, and coffee when confessed to should be corrected. These and other detrimental habits, too individual to enumerate, should receive due attention, the object being, by means of a sensible conduct of life, to bring the bodily functions to a normal state of activity.

Edgecombe¹⁰ writes that his attention has been attracted to a class of cases, suffering from no disease in particular, but complaining of general slackness and want of tone, with a systolic pressure frequently below 100 mm. Hg. (Oliver). He records

⁹ Bull. de l'Acad. de Méd., 1911, 3d series, lxxv, 662.

¹⁰ Practitioner, 1911, lxxxvi, 515.

night and morning readings of systolic pressure in a subject for two hundred consecutive days, and his observations are of great interest. After trying all sorts of remedies in this case, he says the permanent raising of a low pressure is a matter of great difficulty. He has found that a small rise is coincident with marked amelioration, and regards exercise, diet, and change of residence to high altitudes preferable to drug treatment. His subject was a large meat-eater, and he recommends elimination of this staple from the dietary.

To his statement that it is difficult to raise a lowered blood pressure there can be no opposition, and I am also in accord with him when he says small rises in pressure bring about marked improvement of the condition. I am inclined to believe that of all the measures to employ in raising blood pressure in such cases the least to be considered are drugs, although I should be unwilling to abandon the use of strychnine when given in full doses as described above.

THE CLINICAL SIGNIFICANCE OF DIASTOLIC AND PULSE PRESSURE.¹

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IN the last few years the importance and clinical value of determining blood pressure has become recognized and the procedure now stands among the indispensable methods employed in physical diagnosis.

The more recent graduates and certainly all up-to-date clinicians now make frequent observations of the systolic blood pressure; but comparatively few estimate diastolic pressures, and of this number many fail to understand the significance of their observations.

The reason for this is inability to appreciate the significance of or to interpret the diastolic readings is clear.

Until the use of the auscultation method of determining blood pressure was introduced by Karokow in 1905, it was virtually impossible to obtain accurate and uniform diastolic readings outside of a clinical laboratory, where large cumbersome recording instruments were used, so that the wide differences in diastolic readings obtained by different men made any accurate scientific

¹ Read before the Jefferson Hospital Clinical Society, November 21, 1913.

observations impossible. As a consequence, most observers became discouraged and considered diastolic blood pressure readings of no clinical value. Further, there has up to the present time been comparatively little work done on diastolic pressure, so that the clinician has but few observations from which to draw conclusions. Since the advent of the auscultation method, however, it has become a comparatively simple matter to obtain accurate diastolic readings.

The main question now at issue is what constitutes the *true* diastolic pressure when the auscultation method is employed. Is the diastolic pressure represented by the height of the mercury column when the second thumping sound becomes dull or when all sound disappears? For example, after one has applied the cuff of the blood pressure apparatus to the patient's arm and inflated it until all pulsation below the cuff is obliterated, then by releasing the air pressure slowly and listening with the ordinary binaural stethoscope over the line of the artery below the line of the cuff one hears a loud clear thump when the arterial wave first passes the constricting cuff. The height of the mercury column read at this moment indicates accurately the systolic pressure. If one continue to listen over the artery and to release slowly the air pressure, the first thumping sound is replaced by a murmur, which in turn, is followed by a second thumping sound which gradually becomes louder, then fainter, and shortly thereafter disappears. The question under discussion is whether the true diastolic pressure is represented by the height of the mercury column at the time the second thumping sound is loudest or when all sound is gone. At the present writing it has been clearly shown, especially well by the work of Dr. Louis N. Warfield,² that the true accurate diastolic reading should be made at the time the second thumping sound is loudest. It is, however, much easier in most cases to determine the time of disappearance of all sound, which gives a reading approximately 3 to 5 mm. lower. For clinical purposes the disappearance of all sound will suffice, with the exception of cases of aortic regurgitation, in children, in patients with widely dilated arteries, and in high pressure cases where the difference may amount to 8 to 16 mm. of mercury.³

Thus, the determination of diastolic pressures is as easy by auscultation as the making of systolic readings. The auscultation method is the only accurate one by which the general practitioner can determine diastolic pressure.

The sooner clinicians realize that it is impossible to obtain accurate diastolic readings by determining the lowest point of the maximum oscillation of the mercury column or the aneroid needle,

² Interstate Med. Jour., October, 1912.

³ Louis N. Warfield. Jour. Amer. Med. Assoc., October 4, 1913.

and use only the auscultation method, the sooner will we be in a position to obtain a series of accurate diastolic pressures which will be invaluable.

Up to the present time I have been speaking of diastolic pressure readings applicable to adults and older children and have only alluded to infants. In these and small children the auscultation method of obtaining blood-pressure readings is not applicable, as the arteries are so small that the sounds are not distinguishable, and in many cases not audible.

In this class of cases the pith ball indicator first utilized by Fedde⁴ as a diastolic indicator has its place.

The indicator as devised by Fedde afforded no means of determining systolic pressure and, unfortunately, owing to its mechanical arrangement, will not give accurate diastolic readings in infants, though it was applicable to adults.

Later Raymond B. Hoobler⁵ modified this apparatus by using a double cuff and stopcock connection between them in circuit with the pith ball indicator. By this new and ingenious device both diastolic and systolic pressures could be recorded, even in infants.

After considerable work with this apparatus, finding some difficulty in making the readings conform to those obtained by the auscultation method, I changed the mechanical construction of the pith ball indicator so that now the readings correspond exactly with the observations obtained by the auscultation method, where the two methods can be utilized on the same patient.

Before going further it might be well to understand exactly what is meant by diastolic and pulse pressures.

Just as the systolic pressure is an indicator of the force of the ventricular contraction of the heart, so is the diastolic pressure, the pressure existent when the heart and vessels are at rest, an indicator of the amount of peripheral resistance present in the arterial system.

By subtracting the diastolic from the systolic pressure we obtain the pulse pressure, which in turn represents the head of flow. In other words, it represents the excess force the heart exerts over and above the peripheral resistance represented by the diastolic pressure. It is the amount of pressure which carries on the circulation.

The importance of diastolic and pulse pressure at once becomes apparent when it is understood that the first represents the amount of resistance the heart has to overcome to cause the blood to flow, and that the second shows how much excess of pressure the heart is exerting to carry on the circulation.

While the systolic pressure by itself may furnish a great deal of information, it may also be misleading unless checked up with

⁴ Medical Record, July 16, 1910.

⁵ Ibid., December 30, 1911.

the diastolic and pulse pressure. As an illustration: Given a man aged sixty years; on taking his systolic pressure it is found to be 135 mm. Hg.; you naturally conclude that he is a well-preserved man, unless you estimate his diastolic pressure, which, we will say, is found to be 110 mm. Hg. Then the whole picture is changed, you know that the systolic pressure has been much higher, but that the heart muscle has become degenerated, and can no longer maintain the high systolic pressure it should, so that you have the small pulse pressure of 25 mm. Hg. The peripheral resistance indicated by the diastolic pressure of 110 mm. Hg. is high, but the heart cannot maintain a relatively high systolic pressure, so that the pulse pressure is only 25 mm. Hg., instead of about 47 mm. Hg., as it should be, with the diastolic pressure of 110 mm. Hg.

The pulse pressure where the auscultation method is used to obtain the systolic and diastolic pressures should be approximately 35 per cent. of the systolic pressure. In ordinary ranges the pulse pressure is from 25 to 40 mm. Hg.

Recently there has appeared an article by Willard J. Stone⁶ in which he emphasizes the importance of determining the pulse pressure and uses the formula of the pulse pressure divided by the diastolic pressure as indicating the cardiac load. He gives the normal pulse pressure as 50 per cent. of the diastolic pressure, and states that in the severer cases of myocarditis, with failing compensation, the pulse pressure is often greater than the diastolic pressure, which by his formula gives the cardiac load as over 100 per cent. This is a new presentation of the subject of diastolic pressure, and merits extended study and trial.

As more attention is paid to maintaining the normal pulse pressure clinicians will be less ready to administer nitrites to every case of hypertension, as though simply lowering systolic blood pressure would cure them. Much serious injury to many patients will be avoided by observing the fact that as long as in an advanced case there is a normal pulse pressure for a corresponding diastolic reading only harm will come from the use of vasodilators, which lower the systolic pressure and thereby lessen the blood flowing to the various organs of the body.

Often it is simply a question of placing the patient under the best hygienic conditions and maintaining the pulse pressure at about the normal for the corresponding systolic reading. In fact, in advanced arterial conditions, where there are actual arterial changes in the vessel walls the patient's condition is often best treated by the administration of small doses of digitalis and strychnine for their tonic effect on the cardiac muscle and the avoidance of all vasodilators. Since a patient's life should be regulated in accordance with the diastolic and pulse pressures and therapeutics directed to the general cardiac condition.

⁶ Jour. Amer. Med. Assoc., October 4, 1913.

By noting the diastolic pressure and determining the pulse pressure unnecessary stimulation, which would only wear the heart out, can be avoided.

Frequently there is a condition of low systolic pressure due in no respect to cardiac weakness, but to the fact that the arteries and capillaries are widely dilated, as indicated by a low diastolic pressure, the pulse pressure being within a normal range. In these cases, which are often found during the convalescence from a severe illness as pneumonia, influenza, etc., cardiac stimulation is often resorted to because the average practitioner, feeling a small pulse wave or it may be finding the systolic pressure low, immediately concludes the heart is failing and stimulation is required. Nothing could be more erroneous and the stimulation which is not needed simply whips up a heart to beat against a lessened resistance, and the effect produced is similar to that when an automobile engine is allowed to race with all the power on, by releasing the clutch.

In pneumonia one of the most valuable aids in the diagnosis, prognosis, and treatment is the proper determination and interpretation of the diastolic and pulse pressure together with the systolic pressure. The diastolic pressure will often tell whether there is vasomotor dilatation, in which case it will be low, or whether there is a marked venous stasis, in which event the pressure will be high. In the one case vasoconstrictors are called for, while in the other vasodilators or possible venesection is the proper treatment.

Between the pulse rate and the diastolic pressure there is a very intimate relation, well described by Sir Lauder Brunton.⁷

If the pulse is slow more time is allowed for the blood to flow through the arterial system during diastole, and the diastolic pressure is lowered and the pulse pressure increased.

In a weak heart the tension is not raised as rapidly as in a strong one, the pulse is rapid and the time between systoles is shorter and the pulse pressure lower.

In a strong heart the pulse is slower and the intervals between systoles is longer and there is a larger pulse pressure.

When the arterioles contract a high diastolic pressure and a small pulse pressure result, and *vice versa*.

Given a low systolic pressure with a large pulse pressure you probably have a strong heart with dilated vessels.

A low systolic pressure with a small pulse pressure indicates that the heart itself is weak, being unable to maintain the normal pulse pressure. In this case there is usually some dilatation of the vessels, too.

If there is a high systolic pressure and a correspondingly high

⁷ British Med. Jour., November 5, 1910.

diastolic pressure we may assume that there is a normal balance between vessels and heart and that a compensatory condition is present. In all probability there is either an acute or chronic toxic condition, where the high pressure is temporary and will return to normal as soon as the cause is removed, as overeating, etc., or there are arterial, nephritic, and cardiac changes of a permanent character, which not being removable as the damage is already done, can best be treated by conserving the general nutrition of the patient and preventing the development of further changes.

The question is one of balance, it being important to know not so much the pressure the blood is under as the volume of fresh blood delivered to the organs. The actual figures representing the systolic blood pressure may be an aid but they are not important in themselves.

It is essential, in addition, to determine the pulse pressure, as the velocity of flow of the blood stream is roughly equal to the pulse pressure multiplied by the pulse rate. While there are other factors and this is not absolutely accurate in every case, it gives a very good idea of the amount of blood supplied to an organ.

I wish to emphasize the importance of taking the systolic, diastolic, and pulse pressures in every case and impress upon you the ease and accuracy with which this may be attained by the auscultation method.

In taking diastolic readings a great deal depends on the instrument used as well as the method employed.

Three essential qualities of a practical sphygmomanometer have become prominent: (1) Accuracy; (2) portability; (3) durability.

Up to the present time no sphygmomanometer has fulfilled all these requirements.

Some of the mercury instruments have had accuracy and durability, but have lacked portability.

The aneroids, on the other hand, have been portable, but the statements of such prominent physicians as Dr. Richard C. Cabot, Dr. Oscar H. Rogers, chief medical director of the New York Life Insurance Company, and himself the inventor of an aneroid, Dr. J. W. Fischer, Chief Medical Director of the Northwestern Life Insurance Company, Dr. George Oliver, of London, and too many others to mention, have plainly shown the shortcomings of aneroids in point of accuracy and durability.

Realizing the importance of accuracy, portability, and durability, I have devised a new pocket mercurial sphygmomanometer, which I believe embodies all three features named.

It consists of a metal case, which encloses and protects all the glass portions. This makes it durable and eliminates frailty. The lid, when raised, automatically locks in the upright position, and acts as a support for the instrument.

Fig. 1 shows the instrument just after the lid is raised. On the

lid is seenrely mounted by metal clips a cylindrical reservoir (G), partly filled with mercury, into the top of which projects the tortuous tube (F). The top of the reservoir is connected by a union to the metal piece containing the needle-valve (C), the metal connection (B) and the stop-cock (A). The bottom of the reservoir is connected by a U-bend with the glass tube (K), which ends in the steel stop-cock and is fastened to the lid by the metal clamps (I and L). Alongside and parallel to the tube (K) is a folded metal scale (J) which hinges in the middle. At the edge of the lid alongside the glass reservoir is the metal tube (E) containing the glass tube (H) with its ground end.

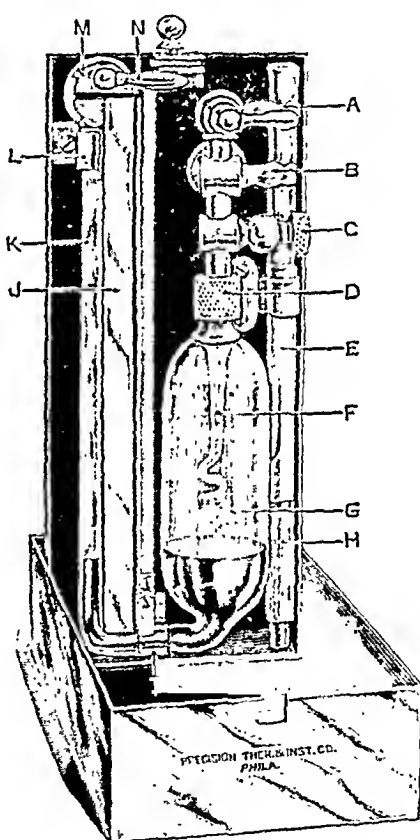


FIG. 1.

To operate, the handle (N) of the stop-cock (M) is raised, the glass tube (H) is removed from its holder, and the ground end inserted through the open stop-cock (M) into the upper end of the tube (K) which is ground to fit it. The scale is then opened by raising the lower end upward. After it is opened the scale is adjusted so that the zero is at the level of the mercury in the tube (K).

FIG. 2. shows how the unions (A' and B') are inserted into the stop-cock (A) and the connection (B) respectively. One should

make sure that the needle-valve is closed and the stop-cock (A) is open as shown in the illustration.

The soft pneumatic cuff is snugly applied to the patient's arm, and the systolic, diastolic, and pulse pressures are accurately obtained by the auscultation method.

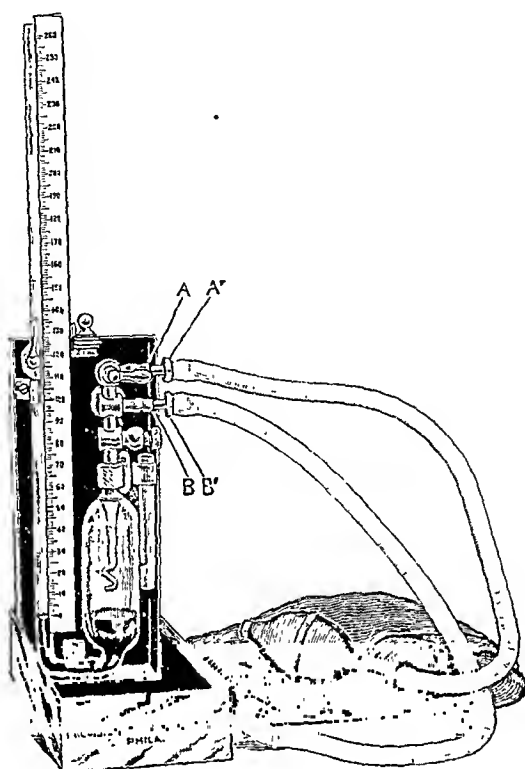


FIG. 2.

One great advantage of this new pocket sphygmomanometer is that by the auscultation method (Fig. 3) the simplest and at the same time the most accurate method of obtaining the blood pressure and the one used by the majority of careful observers, the diastolic pressure is as easily and accurately obtained as the systolic pressure. Also being a mercurial instrument, it is more accurate and dependable than an aneroid, which up to the present is the only other type of instrument that is of equal portability.

The inertia of mercury mentioned as preventing the taking of accurate diastolic readings, has absolutely no significance when the auscultation method is used.

To close the instrument the tube (H) is removed and slid into the metal holder (E). The scale is folded down and then the unions (A' and B') removed. The lid will then be found to close by firm pressure on the upper end. As the instrument is shut the handle of the stop-cock projects beyond the end of the case. This

is so arranged to ensure closure of the stop-cock, to prevent any loss of mercury.

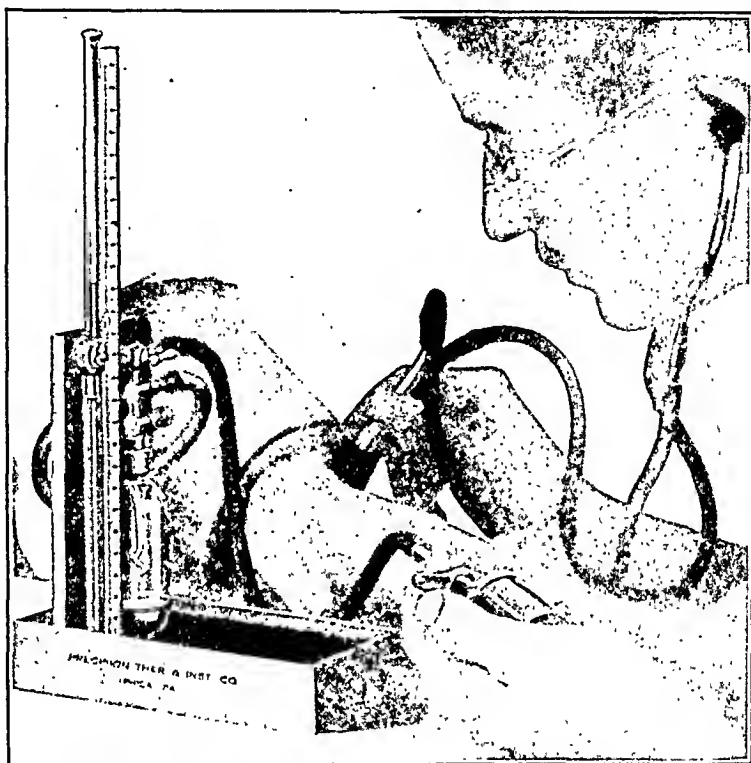


FIG. 3.—The auscultation method.

The instrument fits, when shut, into a morocco carrying-case, the cuff and inflating apparatus alongside it, and after the case is fastened it will slip into the pocket (Fig. 4).



FIG. 4.

ACCURACY. This, the first essential, is obtained in this apparatus by means of the following features: (1) A metal millimeter

scale is used, especially compensated for any lowering of the level in the mercury reservoir. (2) The zero point on the scale is adjustable to the mercury level, so that readings are not affected by climate and temperature. (3) The scale reads directly in millimeters, and being in a vertical line, may be read much more easily than when markings are condensed and on a circular dial. (4) As it is read directly in millimeters of mercury, the primary standard, it does not have to be checked up; one is always sure of the readings; there are no diaphragms to weaken, and there is no delicately balanced needle, actuated by a hair spring. (5) The use of a steel stop-cock and flint glass gives no opportunity for formation of amalgam with the mercury, so there is no black deposit. (6) Redistilled mercury is used. (7) The air release is perfectly even.

PORTABILITY. The entire instrument with inflating apparatus and cuff fit in a morocco carrying-case which slips into the pocket, securing ease of portability. The instrument is so light that it can be readily carried in the coat pocket or in the hand-bag.

DURABILITY. All parts are thoroughly protected by a metal case and are not easily broken or deranged. By a special stop-cock no mercury can be lost. The additional stop-cock (A) is an extra safeguard should the rubber washer in the pump leak a little. Until the washer is replaced the mercury can be maintained absolutely by closing the stop-cock. This is the only pocket sphygmomanometer with this special stop-cock.

In addition the apparatus is simple to operate, it makes use of an accurate, wide, soft cuff which is easily and quickly attached to the instrument by a ground slip joint. An automatic catch on the lid holds the instrument in the upright position when in operation. The mercury remains clean owing to a filter being used, which prevents the powder from the rubber parts being sucked into the mercury reservoir.

This new pocket sphygmomanometer is portable, yet possesses all the accuracy and dependability of the mercury column and is essentially a bedside instrument on which diastolic and pulse pressures can be easily and accurately taken.

THE INHIBITORY ACTION OF CERTAIN ANILIN DYES UPON BACTERIAL DEVELOPMENT.

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SECOND COMMUNICATION.¹

IN a recent communication² we showed that the inhibitory action which certain violet dyes, like gentian violet, methyl violet, Hoffmann's violet, and others, exercise upon certain bacteria is intimately dependent upon the triphenyl methane structure of these dyes and upon the presence of the three amino groups which are found in all the inhibitory representatives of this class. We have also pointed out that the replacement of the basic by acid auxochromic groups or a diminution of the basicity of the respective compounds by the additional introduction of acid groups leads to a loss of this inhibitory power.

In view of the practical as well as theoretical aspects of this problem, it seemed of interest to us to extend our studies to other groups of dyes also, and it is the purpose of this second paper to present the results of these investigations.

DYES INVESTIGATED. Our studies include representatives of the diphenyl amines (that is, of the indamins and indophenols, the oxazines and oxazons, the thiazins and thiazons, and the azins) of the acridins, of the azo dyes, of the hydrazons, of the azobenzidins, of the thiazols, and the oxyquinones.

The general technique was the same as that described in our first communication, the various dyes being used in the concentration of 1 in 100,000 of nutrient agar. The list includes the following representatives, and has been arranged in accordance with their structural composition and their basicity or acidity, the presence of acid or basic groups in addition to the predominating types being represented by arrows pointing in the direction of acidity or basicity respectively.

The organisms examined were for the most part the same as those which had been used in our investigations of the triphenyl methanes.

DIPHENYL AMINES.

A. INDAMINS AND INDOPHENOLS.

Basic.
Phenylene blue
Bindschelder's green

Acid.

¹ Received for publication May, 1913.

² AMER. JOUR. MED. SCI., vol. cxlvii, No. 2, p. 247.

B. AURANTIA.

Aurantia

C. OXAZINS AND OXAZONS.

Capri blue

Muscari—→

Nile blue

New methylene blue

Coelstin blue—→

←—Galloycyanin

D. THIAZINS AND THIAZONS.

Thionin

Methylene blue

Ethylene blue

Toluidin blue

Methylene green—→

Methylene violet

Methylene azure

←—Thioearmin

E. AZINS.

Eurhodins and eurhodols:

Neutral red

Neutral violet

Safranins and safranoles:

Phenosafranin

Tolusafranin

Tannin heliotrope

Amethyst violet

Echt neutral violet

Paraphenylene blue

Indazin

Indulins and indones:

Naphtazin blue

Aposafraanins:

Neutral blue

Basel blue

Indulin R.

Indulin B.

Naphtazin blue (sulphonic
acid derivative)

Rosindulin G.

AZO DYES.

Anilin yellow

Chrysoidin

Vesuvian

Indolin blue

←—Methyl orange

Orange G.

Ponceau

Rocellin

Alizarin yellow

←—Citronin

Dianil red

Dianil blue

←—Dianil blaek

Tartrazin

AZOBENZIDINS.

←—Benzopurpurin

←—Diamin violet

←—Diamin blue

←—Diamin green

←—Pyramin orange

←—Congo red

THIAZOLS.

Primulin

QUINOLINS AND ACRIDINS.

Acridin orange

←—Acid quinolin yellow

OXYQUINONES.

Alizarin red W. S.

Acid alizarin blue

The results which have been obtained with these various dyes in the case of the different organisms that have been examined will be found grouped together in the accompanying tables, the acid dyes being italicized.

Triamino-triphenyl methanes.

	Fuchsin.	New fuchsin.	Acid fuchsin.	Methyl violet.	Crystal violet.	Hofmann's violet.	Denzyl violet.	Dahlia.	Roth violet 5RS.	Iodine green.	Methyl green.	Ethyl green.	Acid violet.	Echt green.
<i>St. aureus</i>	1 0	0	+++	0	0	0	0	0	+++	+++	to +	+	+++	+++
	96 +++	0 to +	+++	0	0	0	0 to +	0	+++	+++	to +	+	+++	+++
	40 +++	0	+++	0	0	0	0	0	+++	+++	+++	+	+++	+++
	95 +++	+++	+++	0	0	0	0 to +	0	+++	+++	+++	+	+++	+++
	42 0	0	+++	0	0	0	0	0	+++	+++	+++	+	+++	+++
	83 +++	+++	+++	0	0	0	0	0	+++	+++	+++	+	+++	+++
	53 +++	+++	+++	0	0	0	0	0	+++	+++	+++	+	+++	+++
	84 +++	0	+++	0	0	0	0	0	+++	+++	+++	+	+++	+++
	58 -	-	-	0	0	0	0	0	+++	+++	to +	+	+++	+++
<i>St. pyogenes</i>	2 0	-	-	0	0	0	0	0	+++	+++	to +	+	+++	+++
	92 +++	+	+++	0	+	+	0	+	+++	+++	+	0	+++	+++
	26 0	-	-	0	0	0	0	0	+++	+++	+++	+	+++	+++
	93 -	-	+++	+	0	-	-	-	+++	-	-	-	+++	+++
	28 0	-	-	0	0	-	-	-	0	-	-	-	+++	+++
	82 -	+++	+++	0	0	-	0	-	+++	-	+	0	+++	+++
	43 0	-	-	0	0	0	0	0	+++	-	0	0	+++	+++
	85 0	0	+++	0	0	0	0	0	+++	+++	0	0	+++	+++
	50 0	0	+++	0	0	0	0	0	+++	+++	+++	0	+++	+++
	81 +	+++	+++	0	0	-	0	+	+++	+++	0	0	+++	+++
	54 +++	0	+++	0	+	+	0	+	+++	+++	+	0	+++	+++
	57 0	-	-	0	0	0	0	0	+++	+++	+++	+	+++	+++
	77 +++	+++	+++	+++	0	+++	0	+	+++	+++	+++	0	+++	+++
	61 0	-	-	0	0	0	-	-	+++	+++	+++	+	+++	+++
	78 -	-	-	0	0	+++	0	0	+++	+++	0	+	+++	+++
	16 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+	+++	+++
	37 0	0	+++	0	0	0	0	0	+++	+++	0	0	+++	+++
<i>St. citreus</i>	47 -	-	-	0	-	-	0	0	+++	-	0	+	+++	+++
	44 0	0	+++	0	0	0	to +	0	+++	+	0	+	+++	+++
<i>M. catarrhalis</i>	6 0	0	+++	0	0	0	0	0	+++	+	to +	+	+++	+++
	100 +++	+	+++	0	0	0	0	0	+++	+++	+	0	+++	+++
	41 0	-	-	0	0	0	0	0	+++	+++	0	0	+++	+++
	75 -	-	-	0	0	-	0	-	+++	-	+	+	+++	+++
<i>M. aurantiacus</i>	9 0	0	+++	0	+	0	0	0	+++	+++	+	+	+++	+++
<i>Anthrax</i>	14 0 to +	0	+++	0	0	0	0	0	+++	+++	+++	0	+++	+++
<i>Actinomyces</i>	15 0 to +	0	+++	0	0	0	0	0	+++	+++	+	0	+++	+++
<i>Pneumococcus</i>	102 0	-	+++	0	0	0	0	0	+++	+++	+	0	+++	+++
	64 +	-	-	+	0	0	0	0	+++	+++	+++	+	+++	+++
	29 +	-	-	0	0	0	0	0	+++	+++	+	+	+++	+++
<i>Meningococcus</i>	71 -	-	-	0	0	-	-	-	+++	+++	+	-	+++	+++
	105 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+	+++	+++
<i>B. typhosus</i>	3 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. paratyphosus</i>	11 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. paratyphosus</i>	12 +++	+++	+++	+++	+++	+	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. paracoli</i>	19 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. coli</i>	32 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. enteritidis</i>	8 +++	+++	+++	0	0	0	-	0	+++	+++	+++	+++	+++	+++
<i>B. dysenteriae</i>	97 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	60 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	68 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	69 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
<i>B. pyocyaneus</i>	70 +++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	7 +++	+	-	0	+	+	-	0	+++	+++	0	-	+++	+++
<i>B. subtilis</i>	4 0	-	-	0	0	0	0	0	+++	+++	0	-	+++	+++
	13 +++	-	-	0	0	-	0	0	+++	+++	+++	-	+++	+++
<i>V. cholerae</i>	20 +++	+++	+++	+++	..	+++	..

		Indaninins.	Aur- antin.	Oxazines and Oxazons.											
		Quinolin yellow.	Acridin orange.	Phenylene blue.	Bind- scheidler's green.	Auran- tina.	Capri blue.	Muscari- n.	Nile blue.	New methylene blue, GGN.	Gallocyanin.	Coccestin blue.	Ultracyanin.	Thionin.	Methylene blue.
St. aureus	1	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	40	+++	+++	+++	+++	+++	+++	+++	+++	0 to +	+++	+++	+++	+++	+++
	96	+++	+++	+++	+++	+++	+++	+++	+++	+	+++	+++	+++	+++	+++
	42	+++	+++	+++	+++	+++	+++	+++	+++	+	+++	+++	+++	+++	+++
	95	+++	+++	+++	+++	+++	+++	+++	+++	0	+++	+++	+++	+++	+++
	53	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	83	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	81	+++	+++	+++	+++	+++	+++	+++	+++	0	+++	+++	+++	+++	+++
St. pyogenes	82	+++	+++	+++	+++	+++	---	---	---	25 0 0	---	0	---	---	---
	92	+++	+++	---	---	+++	+++	+	+	92 0	+++	0	+++	+++	++
	93	---	---	---	---	+++	+++	+	+	0	---	---	---	---	---
	50	+++	+++	+++	0	+++	0	+++	+	+++	---	0	+++	+++	+++
	85	+++	+++	+++	---	+++	0	---	0	0	+++	0	+++	+++	0
	51	+++	+++	+++	---	+++	0	+++	0	0	+++	0	+++	+++	0
	81	+++	+++	+++	---	+++	0	+++	+	0	+++	0	+++	+++	0
	57	---	---	---	---	+++	0	---	+	0	---	---	---	---	0
	77	---	+++	---	---	+++	0	---	+++	---	+++	0	+++	+++	---
	61	---	---	---	---	---	+++	0 to +	0	0	+++	---	---	---	0
	78	---	---	---	---	---	+++	+++	+++	+++	+++	---	+++	---	---
	16	+++	+++	+++	0	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	32	+++	+++	+++	0	+++	+++	+++	+++	+++	+++	0	+++	+++	0
St. citreus	44	+++	+++	+++	---	+++	+++	+++	+	0	+++	+++	+	+++	+
M. aurantiacus	9	+++	+++	---	---	+++	+++	+++	+	0	+++	+++	+++	+++	+++
M. catarrhalis	6	+++	+++	+++	---	+++	+++	+++	+	0	+++	+++	+++	+++	+++
	100	+++	+++	+++	0	+++	+++	+++	+	0	+++	+	+++	+++	+++
	75	---	---	---	---	+++	0	---	---	---	+++	---	+++	---	---
	41	---	---	---	---	+++	0	+++	0	0	+++	---	+++	---	+
Pneumococcus	102	---	---	---	---	---	---	+++	+++	0	+	0	---	---	---
	64	---	---	---	---	---	---	+++	+++	0	+	---	---	---	---
Meningococcus	71	---	---	---	---	---	---	+++	+	+++	+++	---	---	---	---
	105	---	---	---	---	---	---	---	---	+++	+++	---	---	---	---
Anthrax	14	+++	+++	+++	+	+++	0 to +	+++	+++	+++	+++	0 to +	+++	0 to +	0 to +
Actinomyces	15	+++	+++	---	---	+++	0 to +	+++	+++	+++	+++	0 to +	+++	0 to +	0 to +
B. typhosus	3	+++	+++	---	---	+++	+++	+++	+	+++	+++	+++	+++	+++	+++
—α															
B. paratyphosus	11	+++	+++	---	---	+++	+++	+++	+++	+++	+++	+++	+++	0	+++
—β	12	+++	+++	---	---	+++	+++	+++	+++	+++	+++	+++	+++	0	+++
B. paracoli	19	+++	+++	---	---	+++	+++	+++	+++	+++	+++	+++	+++	0	+++
B. coli	32	+++	+++	---	---	+++	+++	+++							

DIPHENYLAMINES (Continued).

		Safranins and Safranoles.					Aposafranins.		Simple azo anilins and Naph-						
		Phenosafranin.	Tolusafranin.	Tannin-helio- trop.	Amethyst.	Echt neutral violet.	Neutral blue.	Basel blue, R. conc.	Rosindulin, 2 B.	Rosindolin, 2 G.	Anilin yellow.	Methyl orange.	Chrysoidin.	Vesuvium.	Orange, G.
St. aureus	1	+++	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++
	40	+++	+++	+++	+++	++ to +	++	++	+++	+++	+++	+++	+++	+++	+++
	42	+++	+++	+++	+++	0 to +	++	++	+++	+++	+++	+++	+++	+++	+++
	95	++	+++	++	+++	0	++	+++	+++	+++	+++	+++	+++	+++	+++
	96	++	++	+	+++	0 to +	+	+++	+++	+++	+++	+++	+++	+++	+++
	53	+++	+++	+	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	84	+++	+++	++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	58	+++	+++	++	+	0	++	+++	+++	+++	+++	+++	+++	+++	+++
	83	+++	+++	+++	+++	0 to +	+++	+++	+++	+++	+++	+++	+++	+++	+++
	93	+	+	++	0	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
St. pyogenes	54	+++	0	0	+++	++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	95	++	++	0	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	92	0	+++	0	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	50	0	+	0	+++	+	+++	+++	+++	+++	+++	+++	+++	+++	+++
	81	++ to +	+++	0	+++	+++	+	++	+++	+++	+++	+++	+++	+++	+++
	77	0	0	0	++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	78	0	0	0	+++	+++	+	++	+++	+++	+++	+++	+++	+++	+++
	37	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	16	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	44	+	+	0 to +	++	0 to +	++	++	+++	+++	+++	+++	+++	+++	+++
St. citreus	44	+	+	0 to +	++	0 to +	++	++	+++	+++	+++	+++	+++	+++	+++
	M. aurantiacus	9	0 to +	+	0	+++	0	++	+++	+++	+++	+++	+++	+++	+++
M. catarrhalis	6	+++	+++	0	+++	0	++	++	+++	+++	+++	+++	+++	+++	+++
	75	+++	+++	+	0	++	++	++	+++	+++	+++	+++	+++	+++	+++
Pneumococcus	41	+	+	0	+	+	+	0	+++	+++	+++	+++	+++	+++	+++
	100	++	++	++	+++	0	+	0	+++	+++	+++	+++	+++	+++	+++
	101	+++	+	+	+	+	+	+	+++	+++	+++	+++	+++	+++	+++
	102	+	+	+	+	+	+	+	+++	+++	+++	+++	+++	+++	+++
Meningococcus	71	+++	+	+	++	+	+	+	+++	+++	+++	+++	+++	+++	+++
Anthrax	14	+++	+++	0 to +	+++	0	+++	++ to ++	+++	+++	+++	+++	+++	+++	+++
Actinomyces	15	++	+	0 to +	++	0 to +	++	++	+++	+++	+++	+++	+++	+++	+++
B. typhosus	3	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
—α															
B. paratyphosus	11	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
—β	12	+++	+++	+++	+++	+	+	+++	+++	+++	+++	+++	+++	+++	+++
B. paracoli	19	+++	+++	+++	+++	++	++	+++	+++	+++	+++	+++	+++	+++	+++
B. coli	32	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
B. enteritidis	8	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. dysenterim	67	+	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	68	+	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	69	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	70	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	90	+++	+	+	+++	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
	91	+	+	+	+	+++	++	+++	+++	+++	+++	+++	+++	+++	+++
B. subtilis	4	+	+	+	+	+	++	0	+	+	+	+	+	+	+
	13	+	+	+	+	+	++	+	+	+	+	+	+	+	+
B. pyocyaneus	7	+	+	+	+	+	++	+	+	+	+	+	+	+	+

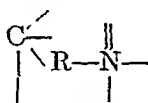
BEHAVIOR OF THE ACID DYES. A survey of these tables will show that not a single one of the acid dyes proper possesses any inhibitory properties in the standard concentration of 1 to 100,000 which we employed. In a number of instances, indeed, we received the impression as though a favoring effect were exercised upon the growth of those organisms, which ordinarily are inhibited by the triamino-triphenyl methanes. This seemed notably the case with tartrazin, a strongly acid hydrazone; then with Ponceau, an azo dye; further with galloeyanin, an oxazon, and the same had previously been noted in one of the triphenyl methanes, that is, roth violet 5 RS. So manifest was this favoring influence in the case of streptococci that the thought suggested itself that tartrazin agar especially might well be utilized for the routine cultivation of these organisms. Even the meningococcus grows in great abundance on this medium, and for a time we were in hopes that it might take the place of serum agar in the case of this organism. We found, however, to our disappointment that while a number of generations may thus be cultivated without any difficulty the organism sooner or later dies out. The observation seemed interesting in principle nevertheless, and seems worthy of further investigation.

BEHAVIOR OF BASIC DYES. While the rule which was found to hold good in the case of the triphenyl methanes thus seems to apply to all classes of anilin dyes, namely, that the presence of acid auxochromic groups *per se* in predominating number over any basic groups is incompatible with the existence of any inhibitory properties, it does not follow, as we have already seen in the case of the triphenyl and diphenyl methanes, that basicity on the part of a dye of necessity carries with it inhibitory properties. We thus find in the present series that toluidin blue, methylene green, neutral red, anilin yellow, chrysoidin, and vesuvin exhibit no inhibitory power whatever in the concentration which we have employed. On the other hand, it will be seen that the majority of basic dyes possess inhibitory power of a kind, but only in a few is this so extensively developed as in the triamino-triphenyl methanes, and is frequently directed only against a certain group of organisms. Basel blue was thus found to be active only in the case of certain catarrhal micrococci, and to a certain extent also in the case of the *Staphylococcus citreus*. The same was noted in the case of diazin blue. Methylene violet affected only the anthrax bacillus, actinomyces, a single strain of the catarrhal micrococcus, and the *Micrococcus aurantiacus*.

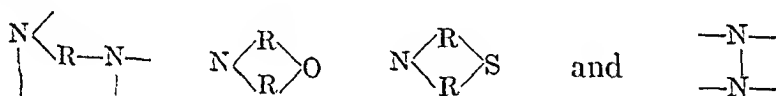
In the case of the triphenyl methanes already it was noted that while some of the dyes were inhibitory for both staphylococci and streptococci, others showed a special selective action for streptococci, while on staphylococci they exercised little or no inhibition. In the groups with which we are dealing in the present

paper this was even more marked, and of the entire number of basic dyes only two were markedly inhibitory for both *Staphylococcus aureus* and streptococci, namely, indazin M and new methylene blue, while echt neutral violet seemed to have a special affinity for staphylococci and azin red, tannin heliotrope, pheno- and tolusafranin, capri blue and coelestin blue, ethylene blue and methylene blue were inhibitory only for streptococci and catarrhal micrococci. As far as the anthrax bacillus and actinomyces are concerned, these were inhibited by practically every dye that had any inhibitory power upon staphylo- or streptococci.

RELATION OF CHROMOPHORIC GROUP TO INHIBITION. The fact that so many of the triphenyl methane derivatives are endowed with inhibitory properties strongly suggests that the underlying chromophoric group, which according to Witt is here the complex



(where R represents a benzene radicle) may be responsible for this effect. The thought, hence, suggests itself that in the other inhibitory dyes of basic nature also the chromophore may be operative in this respect. If further investigation should prove this to be the case, we would be forced to the interesting conclusion on the basis of our own observations that of the enormous number of anilin dyes only those can be expected to have inhibitory properties in which the groups



are represented.

NATURE OF THE INHIBITORY ACTION OF THE DYES IN QUESTION. In considering the nature of the inhibitory action of the dyes in question two possibilities immediately suggest themselves, namely, the existence of a physical as contrasted with a chemical interaction between the dye and the microorganism. As we have shown in our first communication, Stilling inclined to the first possibility, although he felt that chemical influences could not be excluded in the production of the death of the organism. To this view he was without doubt led in great part by the observation that in sufficient concentration the dyes which he had studied would prevent the development of practically all the different bacteria with which he was dealing. But with this phase of the problem we are hardly concerned. On the contrary, we are interested primarily in the fact that in certain dilutions certain dyes will only inhibit the growth of certain organisms. This fact was first pointed out by Rozsahegyi, and was then made the subject

of an extended investigation, in reference to one of the most active dyes in this respect, namely, gentian violet, by Churchman. As a result of his investigations, he divides bacteria into a violet positive and a violet negative group. We have shown that these terms have not been well chosen, since the violet color of the dye has really nothing to do with its inhibiting character, but the fact remains that certain organisms are inhibited by certain dyes, while in others there is no evidence of such an inhibition whatsoever (in the concentration 1 to 100,000 chosen by Churchman and myself as standard). This fact in itself, irrespective even of the important bearing of the basicity or acidity of the dye, makes it seem *a priori*, unlikely that the effects should be of a physical character only. But even more significant in this respect is the fact that certain representatives of a susceptible group of organisms which otherwise present the same morphological and cultural characteristics as the remainder may be dye fast, that is, they are not inhibited by those dyes which interfere with the development of the other members of the same group.

NATURAL DYE-FAST STRAINS. Churchman already noted an instance of this nature, for he mentions that "in a study of five nearly identical strains belonging to the enteritidis group the selective affinity of the stain (gentian violet) was found to be so specific in its nature as to distinguish between different strains of closely related organisms. On the growth of one member of this group the dye exhibited a constant and complete inhibition; on the other four it was absolutely without any effect."

This differing susceptibility of different members of a given group of organisms to a given dye we could establish also in the case of the staphylococci, the streptococci, and the pneumococci. This is illustrated in Table I, in reference to crystal violet agar (sc., serum agar in the case of the pneumococci), 0 indicating absence of growth, \pm faint growth, and $+++$ abundant growth, as in our first paper.

TABLE I.—Showing the behavior of different strains of staphylococci, streptococci, and pneumococci in reference to crystal violet (1 in 100,000).

Staphylococcus aureus.

(1)	(40)	(42)	(53)	(58)	(83)	(84)	(95)	(96)
0	0	0	+	0	0	=	0	0

Staphylococcus Citreus.

(44)

0

Micrococcus Aurantius.

(9)

+ to ++

Streptococcus Pyogenes.

(92)	(26)	(28)	(54)	(43)	(50)	(81)	(77)	(61)	(78)	(16)	(37)
++	0	0	++	0	0	0	0	0	0	+++	0

Diplococcus Pneumonia.

(102)	(64)	(29)
0	+	0

TABLE II.—Showing the behavior of different strains of staphylococci and streptococci toward various inhibitory dyes.

	Staphylococcus aureus.					Micrococcus catarrhalis.		Streptococcus pyogenes.						
	(1)	(40)	(95)	(42)	(53)	(84)	(100)	(6)	(92)	(85)	(50)	(77)	(16)	(37)
Methyl violet	0	0	0	0	0	0	—	0	0	0	0	++	++	0
Crystal violet	0	0	0	0	+	0	—	0	++	0	0	0	++	0
Hofmann's violet	0	0	0	0	0	≠	0	0	++	0	0	++	++	0
Benzyl violet	0	0	0	0 to ≠	0	0	≠	0	0	0	0	0	++	0
Dahlia	0	≠	0	0	0	0	0	0	++	0	0	++	++	0
Fuchsin	0	++	++	0	++	++	++	0	++	0	0	++	++	0
New fuchsin	0	0	++	0	++	0	0	0	+	0	0	++	++	0
Ethyl green	+	+	++	++	++	0	0	+	0	0	0	0	++	0
Brilliant green	++	+	+	0 to ≠	++	0 to ≠	0 to ≠	++	+	0	0	0	++	0
Rhodamin 3B	0	0	≠	+	+	≠	0	++	++	++	++	++	++	+
Rosazoin B	0	0 to ≠	0	0	0	0	0	0	++	++	0	0	++	0
Indazin M	0	++	0 to ≠	0	0	0 to ≠	—	0	0	0	0	0	++	0

This difference in behavior is even more strikingly seen in connection with some of the other inhibitory dyes, as is illustrated in Table II, which likewise shows that even though some of these dyes are closely related, they do not behave in the same manner toward all the strains (see also collective tables).

To explain these individual peculiarities upon a purely physical basis would certainly be difficult, and we are inclined to lay special stress upon this factor as favoring the view that the inhibitory action is of a chemical nature. The likelihood that this may be the case is further emphasized by our observation that it is possible to produce dye-fast strains artificially.

ARTIFICIAL PRODUCTION OF DYE-FAST STRAINS. The observation of Churchman that one single strain only of the *B. enteritidis* group which he had studied was dye-labile, and our own findings of the occasional deviation from what seems to be the normal for a given group of organisms in reference to a given dye, suggested the idea that this aberration might be viewed as a mutation the outcome of special nutritional conditions, and that it should be possible to produce such mutation artificially. We accordingly planted representatives of the different groups of organisms, which collectively were found to be dye-labile upon agar containing the inhibitory dye, in a dilution of 1 in 10,000,000, and increased this gradually (the rate of progress being determined by the activity of the growth) until the 1 in 100,000 standard was reached. A series of experiments of this order and the ultimate results are shown in Table III.

TABLE III.—Showing the gradual adaptation of different organisms to crystal violet.

Behavior toward	<i>Bacillus subtilis.</i> (4)	<i>Bacillus enteritidis.</i> (8)	<i>Staphylococcus aureus.</i> (42)	<i>Staphylococcus aureus.</i> (1)	<i>Bacillus anthracis.</i> (14)
1 in 100,000 (initial) .	0	±	0	0	0
1 in 10,000,000 . . .	+++	+++	+++	+++	+++
1 in 9,000,000 . . .	+++	+++	+++	+++	+++
1 in 8,000,000 . . .	+++	+++	+++	+++	+++
1 in 7,000,000 . . .	+++	+++	+++	+++	+++
1 in 6,000,000 . . .	+++	+++	+++	+++	+++
1 in 5,000,000 . . .	+++	+++	+++	+++	+++
1 in 4,000,000 . . .	+++	+++	+++	+++	+++
1 in 3,000,000 . . .	+++	+++	+++	+++	+++
1 in 2,000,000 . . .	+++	+++	+++	+++	+++
1 in 1,000,000 . . .	+++	+++	+++	+++	+++
1 in 900,000 . . .	+++	+++	++	+++	+++
1 in 800,000 . . .	+++	+++	++	++	+++
1 in 700,000 . . .	+++	+++	++	++	+++
1 in 600,000 . . .	+++	+++	++	++	+++
1 in 500,000 . . .	+++	+++	++	++	++
1 in 400,000 . . .	+++	+++	+	++	++
1 in 300,000 . . .	++	+++	+	+	+
1 in 200,000 . . .	++	+++	+	+	+
1 in 100,000 . . .	++	+++	+	+	±

While these experiments unquestionably demonstrate the possibility of producing dye-fast strains artificially, it must be admitted that the extent to which this is possible is extremely variable. In the case of the subtilis and the enteritidis strain (of the table) it was merely a matter of transplanting daily to the next strength of agar, while with the other three organisms it was sometimes necessary on entering the higher concentrations to allow growth to continue for a few days in the same concentration before advancing to the next. As the end-result shows the degree of adaptation was also quite variable, and in some instances the 1 in 100,000 mark could not be reached.

In this connection it may be interesting to point out that the *B. enteritidis* (8) strain which during the greater part of the winter had been dye-labile ultimately became dye-stable, that is it finally grew quite readily in the presence of all those dyes which in the early fall had inhibited its growth. We cannot help but feel that this change must be viewed as a reversion to what, for that group of organisms, seems to be the normal state. Similarly, we have noted that one streptococcus (16) which originally grew most luxuriantly in the presence of the common inhibitory dyes, is now inhibited by some members of this group (Table IV).

TABLE IV.—Showing reversion of two bacterial strains.

	Original behavior.			Present behavior.		
	Methyl violet.	Dahlia.	Brilliant green.	Methyl violet.	Dahlia.	Brilliant green.
<i>Bacillus enteritidis</i> (8)	0	0	—	++	+++	—
<i>Streptococcus</i> (16)	+++	+++	+++	0	0	0

Upon thinking over the possibilities which have led to this altered behavior we are inclined to refer the change to the fact that whereas during the fall and early winter months the stock cultures of these organisms had been grown on plain agar, they had later been cultivated on beef-juice agar. That apparently insignificant changes in the nutritional surroundings of an organism may actually lead to marked changes in the response of the organism to nutritional stimuli is also shown by an incidental observation which we made when a certain strain of the catarrhal micrococcus had been grown for a comparatively brief period of time on corallin agar and was then transplanted to plain agar and this culture compared with the original (which had not been growing in the presence of corallin). The results are seen in Table V.

TABLE V.—Showing mutation of a catarrhal micrococcus strain under the influence of corallin.

	Methyl violet.	Crystal violet.	Hofmann's violet.
Behavior of original culture (75)	0	0	0
Behavior of culture after having been subjected to influence of corallin (75c)	++	++	+++

If now we attempt an explanation of these various phenomena, namely, the inhibitory action of certain dyes, the existence of natural dye-fast strains, and the possibility of the artificial production of dye fastness, we must bear in mind the fundamental fact that only basic dyes may exhibit inhibitory properties. The most plausible inference, hence, would be to assume the existence of corresponding acid groups in the structure of the organisms in question, with which these basic groups would tend to unite, possibly in a manner corresponding to our concept of the structure of peptids. We could then conceive that the microorganism having anchored the dye in this manner now finds itself unable to bring about the destruction of the molecule with the consequent liberation of that portion which it could utilize in its own metabolism, and the restitution of its own combining receptors. We would thus explain the phenomenon of dye susceptibility upon the same basis upon which Ehrlich explained the action of the toxin molecule upon a cell provided with corresponding receptors, without the necessity, however, of assuming a directly toxic influence. In other words, the cell dies, not necessarily because it has been poisoned, but because a sufficient number of its nutrients have been thrown out of action to bring about its starvation, or inability to multiply, as the case may be. This hypothesis would also explain why an acid dye of otherwise the same structure as the corresponding basic inhibitory dye, even though the same number of amino groups should be present, does not interfere with the growth of the organism. For we could readily conceive either that the dye might be anchored by both its basic and acid groups, or if the latter only should be present, by these alone, and that the attack upon or through this group would lead to the destruction of the molecule, and the liberation of the corresponding receptors. In this connection it may not be out of place to refer to the recent observations by Berthelot and Bertrand³ on the behavior of a certain bacillus, which was isolated by them from the feces, and which was shown to be able either to remove the amino group or the carboxyl group from certain amino-acids and peptids, or both at the same time, according to the nature of the nutritive elements which were otherwise placed at its disposal, showing that the successful attack upon a certain group may lead to the destruction of the nutrient molecule, but that this does not follow of necessity. This is quite in accord with the hypothesis set forth above that the presence of the acid auxochrome group may enable the organism to successfully attack the amino group also, while in the presence of the latter alone this may not be possible. Further investigations will, of course, be necessary

³ A. Berthelot and D. M. Bertrand, Sur quelques propriétés biochimiques du *b. aminophilus intestinalis*, Compt. rend. acad. sci., 1912, cliv. No. 26.

to establish the validity of the explanation which has been offered, but it affords even now a possible explanation, where otherwise it would be difficult to account for the observed facts.

The question, then, whether or not a given organism will be inhibited in its growth by a certain dye would, according to our hypothesis, depend primarily upon the existence of suitable receptors on the part of the organism, and secondarily upon its ability to bring about the liberation of such receptors after once they have been occupied by the dye. To these factors two additional ones should be added, namely, the existence or non-existence of other receptors by which the organism could carry on its nutrition (sc., reproduction), and the possibility of producing such receptors, while the others are occupied by the dye.

Upon the preponderance of susceptible receptors over others, or the relative proportion of these, as compared with others that might serve the purpose of nutrition, the extent of the inhibitory effect would, of course, depend, and account for the divers results that have been obtained in our investigations and which are illustrated in the various tables.

The fact that certain strains of an otherwise dye-susceptible group exist in nature or may be produced artificially would seem to warrant the assumption that such receptors either occur preformed or may be produced artificially, and is in itself a support of our hypothesis, and perfectly in accord with the observations of Ehrlich on the occurrence or production of arsenic-fast strains of trypanosomes. Hitherto we have known but little of the possible existence or production of drug-fast bacteria, and so far as our knowledge goes, Morgenthal's observations on the production of drug-fast pneumococcus strains in the animal experiment are the only ones besides our own which go to show that the principle involved applies not only to animal but also to vegetable organisms.

Should our interpretation of the phenomena under investigation be ultimately proved to be correct in principle, even though not in detail, the chemical nature of the inhibitory action of the dyes would seem to be established. At present we think that the evidence which we have furnished points in that direction.

SUMMARY. 1. The inhibitory action upon the growth of certain bacteria which has been shown to be common to all the triaminotriphenyl methanes is not an exclusive property of this group of anilin dyes, but manifested also to a greater or less extent by other strongly basic dyes, and is dependent upon the presence of basic auxochromic groups and the absence of corresponding acid groups (sc., a preponderance of the former over the latter), in association with the existence of certain chromophoric radicles.

2. Some members belonging to dye-susceptible groups of organisms exist in nature which are not inhibited by the dyes in question.

3. Dye susceptibility may be overcome to a greater or less extent by adaptation.

4. The inhibitory action of the dyes in question is probably due to the existence of corresponding (nutri?) receptors in the microörganism to which the dye is anchored, and its inability to bring about the destruction of the dye and the consequent liberation of the corresponding receptors.

5. Natural or artificial adaptation is due to the production of different receptors by which the nutrition (sc., reproduction) of the organism can be carried on, and which either possesses no affinity for the dye in question, or through which the organism can bring about its destruction.

Since writing the above the artificial production of dye-fast strains of bacteria has also been announced from Ehrlich's laboratory.⁴

DIAGNOSTIC VALUE OF PERCUTANEOUS TUBERCULIN TEST (MORO).

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THE specificity of the cutaneous tuberculin reactions is well established;¹ in other words, it is generally acknowledged that a positive reaction to a tuberculin test indicates a previous tuberculous infection, with the production of tuberculous antibodies. For most clinicians, however, and this apparently applies especially to tuberculosis specialists, the extreme sensitiveness of the reaction, whereby even unsuspected or long-cured cases react positively, militates against its practical importance in clinical medicine. Believing that practically all adults have been at one time or another infected by the tubercle bacillus sufficiently to give a positive reaction, they consider such a reaction to be of little use after infancy and of no value in adult life. For instance, Lawrason Brown says: "A positive reaction (of the cutaneous test) after seven or eight years is of little value, as tuberculous infection and clinical tuberculosis are vastly different." This sentiment is so widespread

⁴ Ueber Gervöhnung d. Bakterien an Farbstoffe. Shiga klin. Zeitsch. f. Immunitätsforsch., vol. xviii, p. 65.

¹ Lawrason Brown, AMER. JOUR. MED. SCI., 1911, cxlii, 469; L. Hamman and S. Wolman, Arch. Int. Med., 1910, vi, 690, et al.

that it is safe to say that, in spite of the admitted value of negative reactions, the use of the various tuberculin tests is not spreading with the rapidity that such valuable diagnostic agents deserve.

Granting that these tests fail to differentiate between the so-called "clinical" and "non-clinical tuberculosis" (an infection never giving rise to noticeable signs or symptoms), we nevertheless believe that the idea that almost all adults will give a positive reaction is erroneous. Whether or not this belief contradicts the theory that almost all adults have been infected at one time or another with tuberculosis, or whether, as some have suggested, it means that a healthy person who has long overcome a tuberculous infection, eventually may lose his sensitiveness so that the positive reaction may "fade"² and eventually change to negative, we are unable to say. The fact, however, remains, as ours and other figures will show³ that in an unselected series of non-tuberculous subjects a small proportion may react positively. It therefore follows not only that the negative reaction with certain definite qualifications practically excludes tuberculosis, but also that the positive reaction is of value, in adults as well as in children, in indicating if not the exhibition of an active course of treatment against clinical tuberculosis, at least an extremely cautious attitude (hygienically and prophylactically) toward the known subject of a tuberculous infection. The unfavorable critique of the tuberculin reactions is well given by M. R. Pla y Armengol.⁴

The following series of 149 cases were seen by us mostly in the wards and out-patient department of the Pennsylvania Hospital during a period of over three years. The Moro⁵ percutaneous test was selected on account of the freedom from infection and discomfort and ease of application. In 128 cases it was controlled by simultaneous applications of the von Pirquet test, applied in the usual manner. This, in the main, agreed with the results of the Moro test, but in a few cases was apparently even more sensitive.⁶ As the chief objection to these tests is their hypersensitivity, this greater sensitivity of the von Pirquet test should be rather considered an objection than an advantage. As the Moro test apparently does not fail to react on tuberculous subjects (with certain known limitations), it would seem to be preferable.

The test was performed substantially as originally described by Moro: a part of the skin free from hair (in epigastrium or hypochondrium), about the size of a silver dollar, is cleaned first with alcohol then with distilled water; one-half the contents of a tube of Moro tuberculin paste (old tuberculin in a base of lanolin, as prepared by

² L. Hamman and S. Wolman, *Arch. Int. Med.*, 1910, vi, 690.

³ F. L. Wachenheim, *Amer. Jour. Dis. of Child.*, 1912, iv, 27, and 1913, v, 466; J. W. Bride, *British Med. Jour.*, May 14, 1910, p. 1161; T. Mills, *ibid.*, p. 1159; M. Pelin, *Lyon Med.*, 1911, cxvii, 945; A. Radziejewski, *Zeitsch. f. Kinderheilk.*, Orig., 1911, ii, 520, et al.

⁴ *Presse Méd.*, 1911, xix, 557.

⁵ *Münch. med. Woch.*, 1908, iv, 216.

⁶ Compare findings of E. Emmerich, *Münch. med. Woch.*, 1908, iv, 1066.

Mulford), about the size of a large pea, is rubbed in vigorously for two minutes. In a similar control area a similar amount of lanolin (the base of the paste) is rubbed for an equal length of time. Both are protected by waxed paper and a dry gauze dressing. In no case was the slightest discomfort, either local or general, experienced. (After the first fifty of these controls had uniformly proved negative the control test was abandoned.) A typical small papular rash (20 to 200) was considered positive; no change as negative; and all other changes as doubtful. If the person administering the test does not react positively himself, it can more conveniently be applied with the bare finger, a rubber finger-cot may be used if preferred.⁷

A positive reaction appeared in the first twenty-four hours in the majority of cases, though in some it did not appear for forty-eight hours; in 2 cases it was negative in forty-eight hours, and typically positive in seventy-two hours; in one case it did not appear until the sixth day. The tests being performed indiscriminately on ward and dispensary patients, were mostly on adults, and therefore constitute a severer trial than if done on children. Before the statistics were arranged, an attempt was made to find out, by mail and by visiting, the subsequent history of the cases, many dating back two and three years. The floating nature of our dispensary population, however, prevented us from reaching more than 12 per cent. The data thus obtained was incorporated in the tables, and was of use in the ultimate diagnosis.

The 149 cases examined have been divided more or less arbitrarily into six classes: three grades of pulmonary tuberculosis (first, incipient or arrested; second, moderately advanced, third, far advanced); other forms of tuberculosis (pleurisy, meningitis, coxitis, etc.); doubtful tuberculosis; and non-tuberculosis (normal and diseases in which tuberculosis could be excluded). The first grade may be assumed to be more or less sensitive (that is, to possess free antibodies which will react to the test), the second still more sensitive; whereas in the third grade the overwhelming infection may be considered so to have exhausted the patient that he frequently is no longer able to produce antibodies which will react to the test. Hence the large proportion of negative reactions in this class. In the last class were put all cases that were definitely non-tuberculous. If any doubt arose, though the tests may have turned out negative, they were included in the doubtful class; conversely, apparently tuberculous cases about which doubt existed were also put in the doubtful class. In diseases like pleurisy, bronchitis, and bronchopneumonia, unless there was a sufficiency of reliable symptoms, such as predominance of certain cells in the

⁷ As one of the authors was found to respond positively to the test, several different samples were tried on him, at various times, and all were found to react positively.

exudate, previous and family history, course of illness, and so forth, the case was put in the doubtful class, always, of course, without regard to the outcome of the test.

TABLE I.—Incipient or Arrested Cases of Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
2	July 14, 1909	Solomon A.	Positive	Convalescent typhoid; dulness and slight deformity of right apex; prolonged, sighing expiration.
14	Aug. 23, 1909	Myer A.	Positive	Von Pirquet also positive; convalescent typhoid; chronic cough; rales and dulness at left apex; brother had tuberculosis.
15	Aug. 23, 1909	Tony Z.	Positive	Chronic cough; rales and dulness at left apex and base.
50	Sept. 20, 1909	Salvatore F.	Positive	Von Pirquet also positive.
80	Sept. 25, 1909	Celia K.	Positive	Von Pirquet also positive; signs of lesion at right apex; lost weight.
86	Oct. 5, 1909	Theresa K.	Positive	Von Pirquet also positive; slight signs at right apex.
112	Mar. 5, 1912	Sam. A.	Positive	Cough; pain in chest; signs at right apex.
113	Mar. 21, 1912	Norman C.	Positive	Von Pirquet also positive; in March, 1913, after continuous outdoor treatment, gained weight; no cough; no signs in lungs.
115	May 4, 1912	Sam. B.	Positive	Cough for five years; signs at left apex.
116	May 7, 1912	Katie J.	Positive	Cough for three years; occasionally chilly and dyspneic.
126	Sept. 3, 1912	Frank C.	Positive	Cough; presteral pain for two weeks; signs at right apex.
134	Aug. 10, 1912	Mary P.	Positive	Fever; cough; rales; loss of weight; improved greatly under treatment; in March, 1913, found at home moribund, general involvement, etc.
137	April 28, 1913	Joseph W.	Positive	Negative on first day; positive on fifth day; signs at right apex; leukocytes, 15,200.
131	Aug. 20, 1912	Alex. S.	Positive	Had pain for three months; cough; rales above and below both apices; dulness at right apex.

14 cases, all positive.

TABLE II.—Moderately Advanced Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
1	July 14, 1909	Joseph D.	Positive	Marked signs at left apex; bloody sputum.
56	Aug. 2, 1909	Jim. C.	Positive	Calmette also positive; right apical lesion with deformity.
70	Oct. 3, 1909	Louis G.	Positive	Von Pirquet also positive; lesion of right lung.
81	Sept. 22, 1909	Costanza C.	Positive	Von Pirquet also positive.
82	Sept. 29, 1909	Minnie T.	Positive	Von Pirquet also positive; rales; dulness at right apex; tubercle bacilli in sputum.
97	Jan. 27, 1910	John J.	Positive	Von Pirquet also positive; cough; fever; diarrhea; signs in lungs.
127	Aug. 14, 1910	Hyman L.	Positive	Diagnosis confirmed at Phipps Institute; in March, 1913, about the same.
135	April 28, 1913	William C.	Positive	Negative on first day; leukocytes, 11,000.
138	May 2, 1913	Frank L.	Positive	Negative on first day; leukocytes 9200 before, 10,200 after.
140	May 2, 1913	Mrs. K. K.	Positive	Negative on first day; leukocytes, 14,000 before, 10,000 after.

10 cases, all positive.

TABLE 3.—Advanced Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
6	July 26, 1909	John S.	Negative	Cavities developed during acute febrile course; confirmed at autopsy two months later.
39	Sept. 4, 1909	Ed. R.	Negative (twice)	Von Pirquet once positive; active and extensive involvement; pulmonary hemorrhage; tubercle bacilli in sputum.
72	Oct. 3, 1909	John C.	Negative	Von Pirquet negative; far advanced with cavities.
85	Oct. 5, 1909	Mattie E.	Negative	Von Pirquet positive; extensive involvement; tubercle bacilli in sputum.
87	Oct. 5, 1909	Katie L.	Negative	Von Pirquet positive; active, extensive involvement, with fever.
90	Oct. 20, 1909	Hattie B.	Negative	Von Pirquet positive; far advanced, with cavities; confirmed at autopsy.
109	Mar. 8, 1912	John S.	Negative	Lost ten pounds; advanced lesions, with death later, at Pennsylvania Hospital.
118	May 11, 1912	Charles H.	Negative	Also spinal tuberculosis; died in two months.
136	April 28, 1913	William C.	Negative	Far advanced in both lungs; leukocytes, 38,000.
139	May 2, 1913	Charles M.	Doubtful	Slight reaction on third day; disappeared on fifth day; leukocytes 22,600 before, 18,000 after.

Of 10 cases, 9 were negative and 1 doubtfully positive.

TABLE 4.—Other Forms of Tuberculosis.

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
3	July 26, 1909	Louis M.	Pleurisy	Positive	Long standing; lymphocytes predominant in pleural fluid.
17	Aug. 23, 1909	Tony R.	Meningitis	Positive	Lymphocytes predominant in spinal fluid; no autopsy.
36	Sept. 4, 1909	Charles Z.	Pleurisy	Positive	Subject to coughs; long-standing osteomyelitis; mother has tuberculosis; protracted case; no fluid obtainable.
42	Sept. 4, 1909	Antonio L.	Pleurisy	Positive	Lost twenty pounds; thickened pleura; lymphocytes predominate.
46	Sept. 14, 1909	John di F.	Pleurisy	Positive	Repeated attacks; reaction slight for forty-eight hours; severe in seventy-two hours.
92	Oct. 20, 1909	Benjamin S.	Meningitis	Positive	Von Pirquet also positive; tubercle bacilli in spinal fluid.
105	Feb. 4, 1910	Salvatore C.	Pleurisy	Positive	Von Pirquet also positive; lymphocytes predominate in pleural fluid.
106	Feb. 2, 1910	Luigi M.	Pleurisy	Positive	Von Pirquet also positive; not tapped; leukocytes, 7440.
131	Aug. 23, 1912	Ettore P.	Pleurisy	Positive	Several attacks of pneumonia (?) and pleurisy; now rubs and dulness on left side; pain and cough; three months later unchanged.
142	May 10, 1913	Stinger (P. G. H.)	Tuberculosis of hip	Positive	Non-febrile; local pain and swelling.

10 cases, all positive,

TABLE 5.—Doubtful Cases.

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
28	Aug. 28, 1909	Thomas M.	Acute pleurisy	Negative	"Never sick before;" in second week of illness eloped from hospital.
44	Sept. 14, 1909	Tony B.	Pleurisy; tuberculous	Doubtful (twice)	Sick one month; cough; pain in side; fever; lymphocytes predominant in pleuritic fluid.
48	Sept. 20, 1909	Harry D.	Pulmonary tuberculosis; myocarditis	Positive	Chronic cough (ten years); lost twenty pounds; x-rays show apical infiltration; von Pirquet also positive.
49	Sept. 20, 1909	Pietro S.	Lobar pneumonia	Negative	Some delay in resolution; von Pirquet doubtful.
52	Sept. 20, 1909	William S.	Pulmonary tuberculosis (?)	Negative	Chronic cough; occult bloody sputum; night sweats; von Pirquet positive; no tubercle bacilli in sputum.
53	Sept. 28, 1909	Peter M.	Acute articular rheumatism; pulmonary tuberculosis (?)	Negative	Right apex slight dulness and prolonged expiration; von Pirquet positive.
55	Sept. 28, 1909	Chianese M.	Pleurisy	Negative	Second attack; slow recovery; lymphocytes about half; von Pirquet positive.
58	Sept. 15, 1909	Sarah H.	Mitral insufficiency; pulmonary tuberculosis (?)	Positive	Fremitus increased below right clavicle with blowing respiration; autopsy refused; von Pirquet also positive.
68	Oct. 2, 1909	John C.	Pleurisy	Positive	Acute onset; rales at right apex; von Pirquet also positive.
69	Oct. 2, 1909	Nick di M.	Pleurisy	Positive	Chronic thickened pleura; von Pirquet positive.
71	Oct. 3, 1909	Charles S.	Pleurisy	Negative	Von Pirquet positive.
75	Dec. 20, 1909	Joe C.	Polyserositis	Negative	Von Pirquet positive.
76	Dec. 20, 1909	Samuel M.	Pleurisy	Positive	Von Pirquet also positive.
83	Sept. 30, 1909	Sarah B.	Bronchopneumonia	Negative	Von Pirquet positive.
96	Jan. 31, 1910	Daniel P.	Chronic dysentery	Negative	Persistent mucosanguineous diarrhea; improved after returning to Italy; von Pirquet negative. No tubercle bacilli in stools.
100	Jan. 27, 1910	Nick P.	Lobar pneumonia	Negative	Delayed resolution; von Pirquet positive.
101	Jan. 27, 1910	Antonio T.	Pleurisy	Negative	First attack lasted two months; von Pirquet doubtful.
107	Feb. 4, 1910	Tony di J.	Pleurisy	Doubtful	Two years later healthy, but has occasional pains in side; von Pirquet positive.
108	Feb. 22, 1912	Sarah W.	Chronic bronchitis	Doubtful	Fever; sweats; cough; seen only twice.
114	April 5, 1912	Boris P.	Pulmonary tuberculosis (?)	Doubtful	Signs at right apex; cough; chills; sweats; eight months later about the same.
120	June 18, 1912	Enibale G.	Pulmonary tuberculosis (?)	Negative	Cough for four months; pain in left axilla; no fever.
121	Aug. 6, 1912	Harry H.	Pleurisy	Positive	Temperature, 99.3°; cough for one month; rubs at left base and side.
123	Aug. 9, 1912	Leo Q.	Pleurisy	Negative	Pain for three months; tapped one month ago; fluid returned.
124	Aug. 30, 1912	Dominie R.	Chronic pleurodynia	Doubtful	Pain in left side, apparently rheumatic; a few large papules after forty-eight hours.
128	Aug. 17, 1912	Benjamin C.	Pulmonary tuberculosis (?)	Doubtful	Dry cough (tonsils and adenoids); unchanged six months later.
129	Aug. 17, 1912	Charles D.	Tuberculous pleurisy	Positive	Pain and dry cough for several years.
130	Aug. 20, 1912	Fred. R.	Acute bronchitis	Negative	Rales soon disappeared; neurotic.
141	May 2, 1913	Mrs. L. H.	Acute bronchitis	Negative	Leukocytes 9600 before test, 5800 after.

Of 28 cases by the Moro test, 15 were negative, 6 doubtful (that is, an atypical or scanty eruption appeared), and 7 positive. In the 16 cases in which the von Pirquet tests were made, 9 negative Moros gave 7 positive von Pirquets and 2 doubtful von Pirquets; 1 doubtful Moro gave a positive von Pirquet. The other 6 tallied. This discrepancy has been commented on above.

TABLE 6.—Non-tuberculous Cases.⁸

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
4	July 26, 1909	Jacob B.	Acute pleurisy	Negative	Quick recovery, polymorphonuclears predominant in pleural fluid.
5	July 26, 1909	Joseph W.	Hemiplegia	Negative	No sign of tuberculosis in history or examination.
7	July 26, 1909	Leon F.	Typhoid	Negative	No sign of tuberculosis in history or examination.
8	July 12, 1909	Charles P.	Malaria	Negative	No sign of tuberculosis in history or examination.
9	Aug. 12, 1909	Lorenzo L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
10	Aug. 12, 1909	John S.	Chronic nephritis	Negative	No sign of tuberculosis in history or examination.
11	Aug. 12, 1909	William S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
12	Aug. 12, 1909	Louis L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
13	Aug. 23, 1909	James D.	Chronic arthritis	Negative	Polymorphonuclears predominant in fluid from knee.
16	Aug. 23, 1909	Pascal D.	Acute pleurisy	Negative	Short attack; polymorphonuclears predominant in fluid from pleural cavity.
18	Aug. 23, 1909	Lawrence C.	Chronic endocarditis	Negative	No sign of tuberculosis in history or examination.
19	Sept. 1, 1909	John Di L.	Plumbism	Negative	No sign of tuberculosis in history or examination.
20	Sept. 1, 1909	James L.	Torticollis	Negative	No sign of tuberculosis in history or examination.
21	Sept. 1, 1909	Joseph C.	Typhoid	Negative	No sign of tuberculosis in history or examination.
22	Sept. 1, 1909	James A.	Typhoid	Negative	No sign of tuberculosis in history or examination.
23	Sept. 1, 1909	Thomas M.	Typhoid	Negative	No sign of tuberculosis in history or examination.
24	Sept. 1, 1909	Steve M.	Typhoid	Negative	No sign of tuberculosis in history or examination.
25	Sept. 1, 1909	Sam L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
26	Sept. 1, 1909	Frank R.	Typhoid	Negative	No sign of tuberculosis in history or examination.
27	Sept. 1, 1909	John A.	Typhoid	Negative	No sign of tuberculosis in history or examination.
29	Sept. 4, 1909	Frank P.	Plumbism	Negative	No sign of tuberculosis in history or examination.
30	Sept. 4, 1909	Angelo M.	Catarrhal jaundice	Negative	No sign of tuberculosis in history or examination.
31	Sept. 4, 1909	William S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
32	Sept. 4, 1909	Nathan F.	Typhoid	Negative	No sign of tuberculosis in history or examination.
33	Sept. 4, 1909	Gennaro D.	Typhoid	Negative	No sign of tuberculosis in history or examination.
34	Sept. 4, 1909	Frank M.	Gastro-enteritis	Negative	No sign of tuberculosis in history or examination.
35	Sept. 4, 1909	William K.	Typhoid	Doubtful	No sign of tuberculosis in history or examination.
37	Sept. 4, 1909	William G.	Asthma	Negative	No sign of tuberculosis in history or examination.
40	Sept. 4, 1909	Nicolo T.	Inguinal hernia	Negative	No sign of tuberculosis in history or examination.
41	Sept. 4, 1909	Joseph S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
43	Sept. 4, 1909	John L.	Lobar pneumonia	Negative	Ran ordinary course, with crisis. No sign of tuberculosis in history or examination.
45	Sept. 14, 1909	John B.	Plumbism; iodism	Negative	No sign of tuberculosis in history or examination.
47	Sept. 14, 1909	Abe T.	Aneurysm of vertebral artery	Negative	No sign of tuberculosis in history or autopsy.
51	Sept. 20, 1912	Louis L.	Paratyphoid	Negative	No sign of tuberculosis in history or examination.
54	Sept. 28, 1909	Paul R.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet doubtful.
57	Sept. 15, 1909	Laura S.	Toxic neuritis	Positive	No sign of tuberculosis in history or examination; von Pirquet also positive.

⁸ Practically all the tests in the acute infectious cases were done in the convalescent stage

TABLE 6.—(Continued.)

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
59	Sept. 15, 1909	Mary S.	Cardiorenal	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
60	Sept. 16, 1909	Clarissa N.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
61	Sept. 16, 1909	Eliza S.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
62	Sept. 18, 1909	Maggie G.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
63	Sept. 18, 1909	Joseph C.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
64	Sept. 20, 1909	Martha T.	Cardiorenal	Negative	No sign of tubereulosis in history or exmination or autopsy; von Pirquet also negative.
65	Sept. 20, 1909	Dominic F.	Acute articular rheumatism	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
66	Sept. 20, 1909	Anna T.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
67	Oct. 2, 1909	Sam. W.	Chronic endocarditis	Negative	No sign of tubereulosis in history or examination or autopsy; von Pirquet also negative.
73	Oct. 3, 1909	Joe F.	Acute bronchitis	Negative	No sign of tubereulosis in history or examination; simple acute attack; von Pirquet negative.
74	Dec. 20, 1909	Pasquale L.	Subacute bronchitis	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative; malingerer (?)
77	Dec. 20, 1909	Sam. B.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
78	Dec. 20, 1909	Leminot B.	Lobar pneumonia	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
79	Dec. 20, 1909	Thomas R.	Lobar pneumonia	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
84	Oct. 5, 1909	Katie S.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
88	Oct. 15, 1909	Maggie O'L.	Acute articular rheumatism	Negative	No sign of tubereulosis in history or examination; von Pirquet positive.
89	Oct. 15, 1909	Maggie P.	Lobar pneumonia	Negative	No sign of tubereulosis in history or examination; von Pirquet positive; ordinary course, with crisis.
91	Oct. 20, 1909	Laura B.	Chronic nephritis	Negative	No sign of tubereulosis in history or examination; von Pirquet negative.
93	Sept. 29, 1909	Mary di M.	Congenital syphilis	Negative	No sign of tubereulosis in history or examination; von Pirquet negative.
94	Nov. 15, 1909	Mary O'D.	Acute bronchitis	Negative	No sign of tubereulosis in history or examination; simple acute case; von Pirquet negative.
95	Nov. 15, 1909	Mary L.	Lobar pneumonia	Negative	Ran ordinary course, with crisis; no sign of tubereulosis in history or examination.
98	Jan. 27, 1910	George F.	Typhoid	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
99	Jan. 27, 1910	John H.	Bronchopneumonia	Negative	No sign of tubereulosis in history or examination; von Pirquet also negative.
102	Feb. 4, 1910	Pat. H.	Lobar pneumonia	Negative	No sign of tubereulosis in history or examination; ordinary case, with crisis; von Pirquet also negative.

TABLE 6.—(Continued.)

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
103	Feb. 4, 1910	Sam P.	Toxic purpura	Negative	No sign of tuberculosis in history or examination.
104	Feb. 4, 1910	James S.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination.
110	Mar. 8, 1912	Jim F.	Chronic constipation	Negative	Very slight slough; no sign in lungs.
111	Mar. 9, 1912	Joseph S.	Acute bronchitis	Negative	Attack cured in three weeks.
117	May 11, 1912	Lily T.	Acute pleurisy	Negative	Cough; pain in chest; friction rubs; first attack; cured in two weeks.
119	June 1, 1912	Leah I.	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
122	Aug. 9, 1912	Frank C.	Acute traumatic pleurisy	Negative	Fell on side three weeks before; pain; cough; rubs all disappeared on second visit, three days later.
125	Aug. 30, 1912	Hyman R.	Debility	Negative	Weak, neurasthenic; no cough or signs in lungs.
133	Aug. 26, 1912	Joe L.	Acute pleurisy	Negative	Cough; pain; rubs in left chest; two days later nothing heard; six months later no sign in chest.
143	May 10, 1913	Bailey (P. G. H.)	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
144	May 10, 1913	Lane (P. G. H.)	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
145	May 10, 1913	Parker (P. G. H.)	Cardiorenal	Negative	No sign of tuberculosis in history or examination.
146	May 10, 1913	Hopkins (P. G. H.)	Senile dementia	Negative	No sign of tuberculosis in history or examination.
147	May 10, 1913	Simmes (P. G. H.)	Acute gastritis	Negative	No sign of tuberculosis in history or examination.
148	May 20, 1913	Carl S.	Normal	Negative	No sign of tuberculosis in history or examination.
149	May 20, 1913	Edward K.	Normal	Positive (twice)	No sign of tuberculosis in history or examination.
150	June 17, 1913	Philip W.	Normal	Negative	No sign of tuberculosis in history or examination.

77 cases, 71 negative (21 von Pirquet negative); of these, one (No. 57) gave both a positive Moro and a positive von Pirquet; one (No. 149) twice gave a positive Moro; two (Nos. 88 and 89) gave negative Moros and positive von Pirquets; one (No. 35) a doubtful Moro, and one (No. 54) a negative Moro and doubtful von Pirquet.

Recently Chiaravallotti⁹ has called attention to the importance of what he calls the "general reaction" following the administration of the cutaneous tuberculin test. He found in most cases of active tuberculosis a distinct rise in the leukocyte count, which he interpreted as a general anaphylactic reaction. For instance, in one case of undoubted tuberculosis he found the blood picture as follows;

	Red blood cells.	Hemoglobin.	Leukocytes.
2 P.M.	3,800,000	70 per cent.	17,200
6 P.M.	3,500,000	70 per cent.	16,000
9 A.M.	3,500,000	70 per cent.	15,800

After von Pirquet test:

2 P.M.	3,600,000	70 per cent.	22,000
6 P.M.	3,600,000	70 per cent.	24,000
8 A.M.	3,500,000	70 per cent.	18,200

⁹ Riforma Med. (Napoli), 1913, xxix, 91.

Though the intrinsic evidence in the above figures might cast some doubt on their value, we nevertheless determined to try out the value of this method. (See cases 135 to 141 in tables.) Owing to the exigencies of dispensary work, one count was made at the same time on successive days. A few cases sufficed to demonstrate its unreliability. In only 1 was the leukocyte count higher after the test than before; in 3 it was lower; and in 1 non-tuberculous case an equally great variation was found. In 3 advanced cases the total leukocyte count was so high (undoubtedly due to mixed infection) that a difference of 2000 and 3000, such as Chiaravallotti described, might easily be due to one of the several factors of error in the technique.

SUMMARY. 1. In 76 unselected non-tuberculous cases only 5 failed to give a negative reaction, and in only 2 of these was the Moro positive.

2. Of 24 cases in the first two grades of pulmonary tuberculosis all reacted positively, indicating as is generally accepted, the specificity of the reaction.

3. Of 10 cases of far-advanced pulmonary tuberculosis, 9 reacted negatively and 1 doubtfully positively.

4. Of 10 tuberculous cases other than pulmonary all reacted positively.

5. Of 28 clinically doubtful cases, by the Moro test 7 reacted positively, 6 doubtfully, and 15 negatively. In the 16 cases in which von Pirquet tests were also made, 9 negative Moro cases gave 7 positive and 2 doubtful von Pirquets, while 1 doubtful Moro gave a positive von Pirquet. The others tallied with the Moro tests.

CONCLUSIONS. 1. In the light of the above figures, reinforced by the opinions of others, we believe to be erroneous the prevalent opinion that positive reactions in adults are of little or no value.

2. The constantly positive reaction in all undoubted early and moderate cases of tuberculosis is a strong indication of the specificity of the reaction.

3. The negative reaction in 90 per cent. of the far-advanced cases indicates that after bodily resistance has been overcome, with the probable disappearance of antibodies, the tissues fail to react to the test.

4. As well as in pulmonary tuberculosis, the test is of value in the differential diagnosis of pleural effusions, joint diseases, abdominal tuberculosis *versus* typhoid, etc.

5. A general anaphylactic reaction, according to Chiaravallotti, as shown by an increase in the number of leukocytes in the peripheral blood following application of the test, is not demonstrable.

6. The test may be repeated on the same patient without alteration of the results. Although in our series the results were in every case the same, rare instances have occurred where repetition produced a different result.

THE SUCCESSFUL REMOVAL OF A TUMOR FROM THE
FRONTAL REGION OF THE BRAIN.

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ALTHOUGH many cases of brain tumor operations have been reported, those in which the successful removal of a neoplasm has resulted in relief of symptoms are still few enough, it seems to us, to make a record of the following case worth while.

Our patient was first seen by Dr. Diller January 20, 1913, having been referred to him by Dr. Guy D. Engle. She was a married woman, aged fifty-three years, of good ancestry, the mother of four healthy children, and had previously enjoyed good health. The first symptom of her present illness occurred August 10, 1912. On this date while she was doing some work in the kitchen, the ring and little fingers of the left hand began to twitch; this twitching gradually extended to the entire hand, the wrist, forearm, and arm successively until the whole extremity was involved in violent convulsive movements which continued for nearly three hours; and at the same time there were twitching movements in the epigastric region. She was conscious throughout the attack. Since this attack the patient has had many similar ones, which at first occurred at intervals of a week or ten days, but recently have become more frequent, and now occur at the rate of about two in a week. These convulsive movements have always been strictly limited to the left arm, and have never involved any other part of the body except upon three occasions, when the epigastric spasms occurred similar to that described. The patient, however, states that for many years in her earlier life she had been subject to such seizures in the epigastric region, and that she had been quite free from them for many years preceding the first convulsion of her left arm. In one of the convulsive seizures (January 13, 1913) she was seen by Dr. Engle, the family physician, who observed that the movements were limited to the left arm and epigastric region. The most severe attack which she has had occurred about ten days before she came under our observation.

After the second arm convulsion the patient noted she could not wring clothes or sew so well as formerly—could not grip so tightly. The arm seemed to her to be growing increasingly numb and weak. About the same time she noted some numbness in the left leg, which had become marked in the previous two weeks;

with the development of this numbness she had noted increasing weakness in the left leg. The patient had never been unconscious in any of these convulsive seizures. She had had occasional attacks of vertigo, but had not been troubled with headache or vomiting, nor had her eyesight failed.

Examination. January 20, (Dr. Diller). The patient's mental condition was good. There was evident weakness of the left hand. Dyn: right, 55; left, 25. The left leg was weaker than its fellow. Pain, contact, and temperature sense in the left arm and leg were normal. Common objects placed in the left hand, such as a watch, bottle, etc., were recognized with a little less certainty and much less promptitude than by the right hand. Knee-jerks: right, normal; left, a little exaggerated. There was no Babinski reflex and no ankle clonus. There was no cranial nerve palsy and no nystagmus. The pupils reacted well to light and accommodation. The eye-grounds were perfectly normal. (Dr. Curry.)

Diagnosis. Here was a case of pure Jacksonian epilepsy involving the left upper extremity and abdomen, the attacks occurring with increasing frequency, and accompanied by a slow progressive paralysis of the left arm and leg and increased knee-jerks on the left side, but by no sensory changes. Headache, vomiting, and optic neuritis—all the major symptoms of brain tumor—were absent. Yet the symptoms pointed strongly to an organic lesion involving the cerebral cortex on the right side and probably irritating chiefly the arm centre. In view of the fact that the convulsive seizures were increasing in frequency and the patient was, especially of late, rapidly losing strength in the left arm and leg, she was advised to go to the hospital and submit to an operation.

She entered the hospital January 21, and was operated upon by Dr. Robert T. Miller, Jr., January 27. During this short period in the hospital, while awaiting operation, she developed no convulsive seizures; however, the weakness in the left arm grew much more pronounced, and at the time of the operation she was practically paralyzed in this member. The left leg had to a less extent also grown weaker.

Operation by Dr. Miller. First operation, January 27, 1913; osteoplastic craniotomy exposing the right motor cortex. Identification of a cortical tumor. Closure.

After etherization a rather large flap was outlined on the skin of the right side of the head corresponding to the underlying motor cortex and a tourniquet of heavy rubber tubing placed about the head. Upon exposure of the bone numerous perforations were made in the line of the incision with the Hudson drill, and by dividing the intervening bridges of bone with a Divilbiss forceps a bone flap was cut out whose undivided base was situated just above the pinna. The skull was extraordinarily thick and seemed unusually vascular, so that the cutting of the flap was a pro-

longed, tedious process and unavoidably attended by so great a loss of blood that even before the flap was turned back it became obvious that extended intracranial exploration was not feasible. Upon breaking up the bone flap the dura was found normal in appearance and under no recognizable tension; a corresponding dural flap was turned back. The exposed cortex seemed at first glance unaltered; the Rolandic fissure and the motor cortex were recognized, though no positive control of this observation was possible because of a lack of the means at hand to stimulate electrically. After a short search, however, there was found in the anterosuperior limit of the exposure a small area of cortex which was slightly paler and definitely softer than the adjoining tissue. In order to investigate this change the overlying edge of bone was rapidly cut out, whereupon it was found that this softened area lay just at the edge of a cortical neoplasm, and was evidently the result of compression. Upon further hurried exposure the tumor was found to be hard, slightly nodular, of a dark reddish-gray color, and sharply marked off from the adjoining cortex; it was situated just anterior to the upper portion of the motor cortex, and extended quite up to the midlongitudinal sulcus of the brain. The pia was densely adherent to the tumor, but the dura was quite free. At this stage of the operation the patient's condition rendered further progress impossible, and a hurried closure was made, with a few buried sutures in the fascia and a continuous silk suture in the skin, a small cigarette drain to the dura being necessary because of the oozing. The urgency of the patient's condition was evidently due to hemorrhage incident to the cutting of the bone flap; hence we hoped for prompt recuperation, and that, at a second operation, within a few days, it would be found possible to expose and remove the tumor—a hope which was fully borne out.

The patient made a prompt and uneventful postoperative recovery. There was only a slight amount of postoperative oozing, so that the drain was removed in forty-eight hours and the drainage tract closed tightly with two interrupted sutures in the skin in order to insure a clean field for the second operation. All sutures were removed on the fifth day. The patient's condition, after her recovery from the operative shock, seemed nowise altered, so that the second operation was undertaken on the seventh day.

Second operation, February 3, 1913. Enucleation of the cerebral tumor previously exposed. Closure.

Without previous cleaning the scalp was thoroughly painted with tincture of iodine, the osteoplastic flap turned back, and the cortex exposed and covered with a cotton compress saturated with warm normal salt solution; no anesthesia was needed up to this point. The patient was now etherized and the overlying bone rapidly cut away until the tumor was completely exposed. It was necessary to carry the craniectomy slightly past the midline at

one point. The tumor presented the same appearance as at the first exposure; its long axis was approximately 5.5 cm., running anteroposteriorly, and its width was about 3.5 cm. The situation of the tumor was just anterior to the extreme upper portion of the motor cortex, where it lay snugly tucked in between the falx cerebri and the right hemisphere of the brain. Attempt was now made to remove the mass by a slow dissection, with division of the cortical vessels between ligatures; but even a slight dislodgement resulted in so free a hemorrhage from the obscured region at the base of the tumor that this method had to be abruptly abandoned in favor of the more rapid enucleation with the finger. The tumor seemed well encapsulated and separated readily and cleanly from the brain tissue. As the falx was approached beneath the tumor the finger encountered slight though definite resistance, suggesting a pedicle attaching the mass to the deep edge of the falx near the corpus callosum. This suspicion was promptly confirmed, for simultaneously with the separation of this pedicle and the removal of the tumor the cavity was filled with the blood of a profuse venous hemorrhage. The bleeding was controlled by pressure, and after the field was cleared there was found at the deep edge of the falx a roughened lacerated area, from which the blood poured in a heavy stream. Evidently the pedicle was attached to the wall of the inferior longitudinal sinus, which had been torn during the process of enucleation. Difficult exposure and loss of blood ruled out any prolonged attempt to excise or suture this portion of the wall of the sinus. A small pledget of cotton, moistened in normal salt solution, was applied accurately to the rent in the sinus wall and held in place a few minutes, when, upon removal of the pressure, the cotton pledget alone was found to control the bleeding perfectly. A small cigarette drain was led to this pledget and the dura partially closed with a few interrupted sutures, the bone flap replaced, and the closure completed with a few interrupted sutures in the fascia and a continuous silk suture in the skin. The loss of blood during the operation of a little over an hour had been considerable, and the patient left the table in well-marked shock.

During the first eighteen hours after the operation the patient's condition was decidedly unpromising, with a pulse ranging from 120 to 160, and irregular at times; but after that she steadily improved, and subsequently passed through a satisfactory convalescence. The highest temperature was 101.4° eight hours after the operation, and for ten days there was a slight evening rise. The drain was removed on the fourth day and the skin approximated with sutures, as after the first operation. By the sixth day all sutures except those just mentioned were removed: the wound healed *per primam*, except for a minute opening in the anterior limb of the incision, from which there was a slight

drainage of clear cerebrospinal fluid for seven days. During the first five days the patient exhibited intermittently a mild delirium.

For the pathological report on the tumor, and the accompanying photograph we are indebted to Dr. A. T. Henrici, pathologist to St. Francis Hospital:

Macroscopic Description. The specimen consisted of a tumor mass measuring 4.5x3.5x3 cm. It was oval in outline and the surface was nodular. The tumor was everywhere covered by a smooth lining membrane, save on one side, where there was a small round depression having a roughened surface, indicating the point at which it had been detached from its pedicle. On section it is seen to be composed of small round masses the size of peas or larger, separated from each other by narrow bands of loose edematous stroma, which frequently showed hemorrhage. The tumor thus had a lobulated appearance. The tissue composing the lobules had a smooth, glistening white cut surface, showing occasional minute hemorrhages. It was moderately firm.



Photograph of tumor removed.

Microscopic Description. Sections of the tumor showed a vascular structure. Some areas were composed entirely of closely aggregated vessels and blood-spaces. Other areas had a more solid appearance, but on examining them with a higher power they were seen to be composed of similar closely aggregated capillaries, which had become collapsed, so that their lining cells had come into closer relationship with each other and gave the appearance of a solid tissue. Still other areas, which formed the greater part of the tumor, were composed of dense masses of cells compactly arranged. These cells were rather large, rounded, oval, or spindle-shaped cells, having large deeply staining nuclei and a rather indefinite, faintly staining protoplasm. Their nuclei occasionally showed mitotic figures, but these were by no means frequent. The cells showed no fibrils with phosphotungstic acid hematoxylin. They were the same as the cells which lined the capillaries noted above. Occasional vessels were noted which had a well-defined muscular wall; but for the greater part the vessels existed as mere blood-sinuses, having no other lining than the tumor tissue itself. The tumor was supported by a rather small amount of dense connective tissue. In places heavy bands of stroma were noted.

Diagnosis. Hemangio-endothelioma of the dura.

COMMENTS (Dr. Diller): Following the second operation the patient was completely paralyzed in the left arm, face, and leg. Within a few days she regained power in her face. Three weeks later she began to get some strength in her leg; and after a period of six weeks some motion in the arm and shoulder returned. At this writing the patient is slowly gaining strength in both arms and legs. She is now able to walk without assistance. The arm is still weak, although gaining slowly and steadily.

This case is interesting from several points of view. Here was a growth of fair size which produced none of the well-known symptoms of brain tumor, but which manifested itself chiefly by Jacksonian epilepsy involving the left arm and by a slowly progressive hemiplegia. This tumor, situated just anterior to the right motor cortex, and lying between the falx and frontal lobe, would naturally be expected to produce symptoms referable to the trunk and leg rather than the arm. Yet from the onset there appeared to have been convulsions of the muscles of the upper abdominal wall accompanying those of the arm while the leg itself was never involved in convulsions. We were somewhat led astray in supposing the lesion chiefly located in the arm centre. The movements in the epigastric region we found difficult to interpret, since they occurred with only two or three of the arm convulsions; moreover, we had the patient's history that similar attacks had occurred over a period of many years running back to childhood. We were, therefore, disposed to eliminate these attacks from consideration as evidence pointing to localization of the lesion. Even now it is difficult to interpret them. If one considers these early epigastric convulsions indicative of a lesion in the frontal cortex involving the adjacent centre for the trunk there is great difficulty in explaining the long history, the disappearance of these convulsions for several years and their subsequent reappearance with the onset of trouble in the left arm. The patient also described these epigastric movements as definitely limited to that region of the body, and it was felt that this manifestation, whatever it indicated, was probably not related to the arm convulsions and hemiplegia.

From a practical point of view it will be seen that the old-fashioned trephining operation with an exposure of merely the middle Rolandic area would have failed to demonstrate the tumor; the value of a large osteoplastic flap is well illustrated.

This case also illustrates the practical point that a tumor may declare itself in an irregular and unusual manner. Besides the absence of general symptoms of brain tumor already referred to, the Babinski toe reflex and ankle-clonus, which one might expect to find, were both absent in this case. The knee-jerk, however, was distinctly increased, as compared with its fellow, and was a diagnostic sign of considerable value.

THE TOTAL NON-PROTEIN NITROGEN OF THE BLOOD IN PREGNANCY AND ECLAMPSIA.¹

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In the course of some recent work on the non-protein nitrogen ("rest" nitrogen) content of the blood in nephritis,² we had the opportunity to examine specimens from a number of patients suffering from eclampsia. As the results obtained in these few cases seemed to promise information of value, we collected additional material, and now present our findings in some twenty pregnant women, one-third of whom were normal while the remainder presented toxic phenomena of one sort or another. For the determination of the total non-protein nitrogen and urea of the blood we employed the technique recently perfected by Folin.³ Only 5 or at the most 10 c.c. of blood are required, an amount readily obtained from a vein by a syringe. Strauss⁴ has recently combined the method of collection and precipitation of the blood devised by Folin, with the ordinary Kjeldahl determination of the nitrogen, which may possibly be a fairly satisfactory procedure for the detection of gross variations when the special apparatus for the Folin method is not available. So far as we can ascertain no one has yet published a series of cases by the improved method we have employed, nor are data of any sort with reference to the nitrogen or urea of the blood in pregnancy available in any quantity.

Landsberg⁵ examined the oxalated blood-plasma in a series of 18 pregnant women, clinically normal, and found, by the Kjeldahl method, the average content of "rest" nitrogen to be 24 mg. per 100 c.c. In 10 parturients the average was 23 mg., while in 8 normal non-pregnant women the average was 21 mg. per 100 c.c. In 1 case, however, in which the pregnancy was complicated by edema, albuminuria, and cylindruria the blood-plasma obtained

¹ Read before the Pathological Society of Philadelphia, October 9, 1913.

² C. B. Farr, and J. H. Austin, The Total Non-protein Nitrogen of the Blood in Nephritis and Allied Conditions, *Jour. Exper. Med.*, 1913, xviii, 228.

³ Newer Methods for the Determination of Total Non-protein Nitrogen, Urea, and Ammonia in the Blood, *Jour. Biol. Chem.*, 1912, ii, 527.

⁴ Zur Prognosestellung bei Nephritis, *Zeitsch. f. Urol.*, 1913, vii, 287.

⁵ Untersuchungen ueber den Gehalt des Blutplasmas an Gesamteiwass, Fibrinogen und Reststickstoff bei Schwangeren, *Archiv. f. Gynak.*, 1910, lci, 693.

ten days before delivery showed a content of 276 mg., a very considerable increase over normal.

Zangemeister⁶ bases his figures on the 9 cases of eclampsia which he examined by a similar method, and found them to range between 15.7 and 44.3 mg., with an average of 25.8 mg. per 100 c.c. He determined the freezing-point of the plasma and reached the conclusion that, "As a rule 'rest' nitrogen is somewhat increased in eclampsia dependent upon the molecular concentration of the blood. There are single cases, however, in which this increase fails, even although the cases may have further convulsions. This increase should not be considered as a cause of eclampsia, but rather a secondary appearance, due to a lowered diuresis." In this connection it may be stated that Strauss has found no definite relation between the nitrogen content and the depression of the freezing-point.

Herter⁷ in an article which does not give his actual figures or methods, states that in his study of the blood in six cases of eclampsia there was no increase in the percentage of urea. In a subsequent paper he⁸ concluded that in cases of eclampsia without chronic nephritis the percentage of urea in the blood was almost regularly normal or only slightly increased in amount. When chronic nephritis existed the urea was apt to be high, and when this was the case a fatal outcome was to be expected.

In the following table we have classed our cases in four groups. Group A includes seven cases of normal pregnancy. The total non-protein nitrogen ranged from 21 to 31 mg. per 100 c.c., while the urea (or more precisely the ammonia-urea fraction) varied from 7 to 15 mg. per 100 c.c. of whole blood. These figures we consider perfectly normal, and this is confirmed by the other tabulated data, with the exception, perhaps, of the phenolsulphonephthalein test, to which we will refer subsequently.

Group B consists of three cases, in which the most prominent symptoms were referable to renal insufficiency; in one case valvular cardiac disease was added as a complicating factor. In each of these cases the pregnancy was interrupted on account of the increasing severity of the symptoms. In these cases the total non-protein nitrogen ranged from 34 to 52 mg. per 100 c.c. and the ammonia-urea fraction from 11 to 30 mg. per 100 c.c. of whole blood. The estimations were repeated in 2 of these cases during the puerperium; in 1 case a slight and in 1 case a considerable decrease was found. It will also be noticed that the decrease was practically all in the urea. In 1 case the history suggested chronic nephritis, and the urine contained albumin and casts when the patient left the hospital.

⁶ Untersuchungen ueber die Blutbeschaffenheit und die Harnsecretion bei Eklampsie, *Zeitsch. f. Geburtsh. u. Gynak.*, 1903, i, 385.

⁷ The Pathology of Uremic Intoxications, *Montreal Med. Jour.*, 1898, xxvii, 321.

⁸ C. A. Herter, On Urea in some of Its Physiological and Pathological Relations, *Johns Hopkins Hospital Reports*, 1900, ix, 69.

GROUP A—CASES CLINICALLY NORMAL.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts
						1st hour	2d hour	total				
1	22	II	5th	20	6	120	none	none	none
2	27	II	9th	23	10	21	11	32	140	none	none	none
3	21	I	9th	25	8	25	3	38	125	none	trace	none
4	25	I	7th	27	14	125	none	none	none
5	27	IV	7th	30	13	130	slight	trace	none
6	16	I	9th	28	14	25	25	50	130	none	trace	none
7	19	I	8th	27	10	28	19	47	140	none	none	none

GROUP B—CASES WITH RENAL SYMPTOMS PREDOMINATING.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts
						1st hour	2d hour	total				
1	37	I	5th	33	16	15	9	24	175	Ex- treme	Heavy cloud	Hya- line gran- ular
1	37	I	10 days after delivery	29	160	Slight	Trace	Ocas- sion- ally
2	39	II	9th	52	30	20	15	35	204	Mod- erate	Light cloud	Hya- line gran- ular
2	39	II	14 days after delivery	29	7	23	12	35	195	None	Trace	None
3	20	I	9th	35	11	19	15	34	165	Mod- erate	Heavy cloud	None

GROUP C—CASES WITH ECLAMPTIC CONVULSIONS.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts	Notes
						1st hour	2d hour	total					
1	18	I	1 day post partum	25	11	32	20	52	160	none	Trace	None	
2	24	II	8th	37	25	20	195	Marked	Heavy cloud	Hya- line gran- ular	Died
3	29	III	9th	40	27	0	0	0	210	Slight	Heavy cloud	Hya- line gran- ular	Died
4	23	I	1 day post partum	46	30	35	20	55	162	Slight	Heavy cloud	Hya- line gran- ular	
4	23	I	14 days post partum	35	14	140	None	Trace	None	
5	19	I	9th	54	..	20	3	23	165	Marked	Boiled solid	Gran- ular	
5	19	I	11 days post partum	25	11	25	20	45	140	None	Light cloud	None	
6	30	I	7th	51	22	20	18	38	210	Slight	Light cloud	Gran- ular	
7	29	I	6th	72	50	180	Marked	Light cloud	Gran- ular	Died

GROUP D.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts	Notes
						1st hour	2d hour	total					
1	24	II	3d	22	8	50	18	68	116	Slight	None	None	Salivated
2	32	II	8th	23	11	160	Slight	None	None	Headache
3	30	III	8th	20	8	30	10	40	130	None	None	None	Retinitis Chorea

Group C includes seven cases presenting convulsions as a prominent clinical symptom. The eclamptic seizures varied in number and severity. One case, the first in this group, after a normal delivery had a typical eclamptic convulsions further attacks were avoided by immediate treatment. In this instance the total non-protein nitrogen was within normal limits, 26 mg. In the other cases the figures ranged from 38 to 72 mg.; both patients represented by these extremes died, but several showing intermediate values recovered. Of the latter two were examined again after they had made clinical recoveries, and in each a considerable reduction in the nitrogen was found.

It will be noted that the other laboratory findings were in the most part confirmatory.

Group D comprises three dissimilar cases: one of uncontrollable vomiting during the third month of pregnancy; one of persistent headache, hemorrhagic retinitis, and high blood-pressure, without urinary changes; and one in which the pregnancy was interrupted at the eighth month on account of a chorea of increasing severity. In none of these cases was there any increase either in the nitrogen or in the urea, the former ranging from 21 to 24 mg. per 100 c.c. and the latter from 8 to 12 mg. per 100 c.c. of whole blood. In the first case the vomiting ceased after admission to the hospital, but marked salivation persisted for some time. In the second case the symptoms improved after rest in bed, and practically disappeared after delivery. In the third case the outcome was also satisfactory.

In 15 out of the 20 cases the functional efficiency of the kidneys was estimated by the phthalein test of Rowntree and Geraghty. In general there was a tendency to slightly subnormal values even in normal cases; in the pathological cases there was usually a correspondence between the nitrogen retention and the diminished phthalein excretion. In one case, however, the nitrogen fell rapidly, with clinical improvement, but there was no rise in the phthalein elimination. The amount of non-protein nitrogen retained is probably an index of the temporary degree of toxemia

(uremia literally), while the phthalein elimination is an index of the excretory efficiency of the kidneys. In our normal cases the two-hour elimination ranged from 32 to 50 per cent.; in the cases with renal symptoms, in Group B from 24 to 35 per cent.; and in the eclamptics from 0 to 52 per cent. In the last group the figures were far from consonant with the clinical symptoms—that is, if we suppose the latter to be due in any way to renal inadequacy.

Turning to the literature we find that Sondern and Harvey⁹ in a series of 18 pregnant women, clinically normal, determined an excretion of phthalein of from 21 to 58 per cent. in two hours, with an average of 45 per cent.; 1 case with a true renal lesion having convulsions, eliminated 24 per cent; 1 case in which albumin and casts disappeared from the urine shortly after delivery eliminated 38 per cent. Goldsborough and Ainley in normal pregnant¹⁰ women found the excretion to vary between 13 and 67 per cent, with an average of 47 per cent. In the puerperium the figures ranged from 48 to 76 per cent., with an average of 61 per cent. Both averages are below that of healthy non-pregnant individuals. Erne¹¹ in two normal pregnant women found 70 and 72 per cent. of the phthalein eliminated; in a case of eclampsia at the fourth month of pregnancy, two tests showed 62 and 70 per cent. respectively. A case of renal disease in a pregnant woman showed 42 and 44 per cent. on two examinations.

The blood-pressure in Groups B and C showed a definite increase above the normal in all cases; in no case was the systolic pressure less than 160 during the acute stage. In the remaining normal and miscellaneous cases the blood-pressure was 140 or less in all, with one exception already noted. The urinary changes were also strictly consistent with the clinical symptoms.

CONCLUSION. In normal pregnant women the total non-protein nitrogen does not usually exceed 30 mg. per 100 c.c. of whole blood. In general hospital cases without demonstrable renal lesions it may frequently reach 40 mg. or more. Slighter disturbances of function are therefore more clearly defined in the former class.

In all cases of pregnancy in which there was definite renal insufficiency or eclampsia, with one exception, there was always a slight and in most cases a considerable increase in the total non-protein nitrogen. The degree of retention was similar to that found in parenchymatous nephritis rather than the higher grade common in the interstitial variety. It bore no definite relation to the severity of the symptoms. In only one case did the figures reach

⁹ The Phenolsulphonephthalein Test for Estimating Renal Function in Pregnancy, Bulletin of New York Lying-in Hospital, 1912, viii, 172.

¹⁰ The Renal Activity in Pregnant and Puerperal Women as Revealed by the Phenolsulphonephthalein Test, Jour. Amer. Med. Assoc., 1910, lv, 205S.

¹¹ Functionelle Nierenprüfung mittels Phenolsulphonephthalein nach Rowntree und Geraghty. Münch. med. Woch., 1913, lx, 510.

a height which, according to Strauss,¹² would suggest a dubious prognosis. This patient died; another, with much less retention, also died.

The relatively normal elimination of phthalein in some cases of eclampsia and the markedly lowered excretion in some clinically normal cases will not permit us to draw any conclusions as to its real diagnostic or prognostic value from this brief series.

The presence of a rising blood-pressure, the condition of the urine as regards albumin and casts, and the clinical picture are severally more important than either of the newer methods we have employed. Further experience may modify this view, for Widal considers the examination of the blood of greater prognostic, if not diagnostic, value than the examination of the urine.

We are indebted to Dr. R. C. Norris for the privilege of studying in this connection several interesting cases at the Preston Retreat.

PROLAPSE OF THE OVARY: ITS RATIONAL MANAGEMENT.

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ANY prolapse of the ovary, as a distinct, clearly defined, and well-recognized entity, is a morbid condition of a not uncommon occurrence. That this organ of the female sexual system can be so displaced must be apparent to all observing gynecologists.

The left ovary, experience teaches us, is more frequently so disordered. Thus, firmly connected with the uterus by the short, stout, fibrous ovario-uterine ligament, it must, by forces of necessity, in the normal movements of the body, be altered somewhat in its position in various directions; and situated normally on the posterior and upper surfaces of the broad ligament, it is also put in intimate association with the physiological position and condition of the rectum, namely: its distentions as a reservoir for fecal matter and a channel for its evacuation. The physiological movements of the human body in daily life necessarily imply many alterations in the posture of the pelvic viscera to a varying degree. The wise dispensation of nature that an ovary can materially change its position without any derangement of its sensation or function is one of the many provisions of our created organization.

A displacement of any of the internal genitalia of the human female is then a morbid entity only when these alterations in position are persistent and unalterable by natural efforts, and when

¹² Loc.cit.

they become the sources of pelvic discomfort and constitutional disturbances.

Any displacement of the internal genitalia may be primary or secondary. Primary, when this alteration has no antecedent pathological change; secondary, when such morbid variations do exist.

Primary displacements are usually traumatic in origin and precipitous in action; secondary, are slow and insidious in causation, and gradual in manifestation.

Without doubt some cases are congenital, occurring in the formative stages of genital development.

Most cases of ovarian prolapse are secondary, and are necessarily aggravated by individual, coexistent, or antecedent conditions. These pathological changes partake of various varieties and degrees.

In the consideration of uterine displacements we classify these causes into : (a) those attributable to an increased bulk and weight of the organ; (b) those resultant from some relaxation of the normal supports; (c) those dependent upon an increased abdominal pressure from above; (d) those arising from abnormal tractile forces from below. So with the ovary. Two or more of these causes may be operative in the same case.

It is unnecessary to enter further into the special causes, contributing to an increased bulk and weight of the ovary, or to the underlying conditions favoring some relaxation of support. There is always some elongation of the suspensory or the infundibuliform pelvic ligament in such cases.

In this consideration of the subject of ovarian prolapse, we desire to have our remarks referable only and distinctly attributable to conditions in which the ovary is the only offending organ, and not to cases associated with, or dependent upon, backward or downward dislocations of the uterus.

Backache and sensations of pelvic weight and heaviness are ordinarily present, especially at the periods of ovulation and menstruation, owing no doubt to an intrapelvic physiological turgescence of blood-supply at this time. More pronounced and characteristic symptoms are pain during defecation, continuing, it may be, for hours after unless the stools are free and soft. Sexual intercourse is always painful, for the reason that the ordinary completion of this act implies more or less contusion of this displaced and tender organ.

There is usually menorrhagia and dysmenorrhea also.

The anatomical fact that the right ovarian vein empties obliquely into the ascending vena cava, while the left ovarian vein has its outlet at right angles into the renal vein, is one of the reasons why the left-sided organ is more inclined to have an obstructed venous circulation, and becomes, in consequence, more often the seat of some pain, with many of its structural lesions.

There are varying degrees of prolapse. To be unmistakably noticed, the utmost displacement must be present, that is, the ovary lies at the bottom of Douglas's fossa.

Constitutional symptoms are such as are usually manifested in many female pelvic diseases. In the main, both local and general symptoms are dependent on the vicissitudes of female life, with its many changes of pelvic circulation of an active or passive kind.

The diagnosis is easy, yet it may be confounded with a retroflexed uterus, with an extra-uterine fibroid, situated on the posterior uterine wall, or with the presence of a chronic pelvic inflammatory exudate. A careful bimanual method of examination of the vagina and rectum makes clear the nature of the case. From the first condition, it can, if needed, be safely differentiated by the gentle insertion of a thoroughly sterilized, flexible, copper uterine sound, followed by rest; and, from the latter, by the careful history of the case, and by the continuance, if not the persistency, of the retro-uterine morbid mass, unaltered by taxis, with the patient in the knee-elbow posture.

A prolapsed ovary is at times a tender, pulsating body—the most disturbing cases.

The most important of all things, in a practical sense, consists in the complete and permanent rectification of the displaced ovary, a condition which, if neglected, surely will sooner or later lead to a general disarrangement.

In the first place strict attention must be given to obtaining daily by diet, and by medicine if necessary, a full, free, soft, easy evacuation of the intestinal tube—the most important sewer, of the human body. For the most part the salines or the sulpho-saline mineral waters answer this purpose well during the summer months.

Occasional small doses of calomel (gr. $\frac{1}{10}$ each), followed by phosphate of sodium or sal Rochelle or Pluto Water, or a laxative pill of podophyllin, belladonna, and nux vomica, also accomplish this end at any time. The following rule should be observed: To take an appropriate dose of either, at night on retiring, or early the following morning fasting, provided the requisite movement of the bowels has not been obtained the previous day.

The avoidance of constipation not only cleanses the system, but it aids digestion; it gives less work for the kidneys to do, in the way of systemic elimination; it clears the skin and it promotes mental and bodily activity. How many women have obtained thereby a complete relief from repeated attacks of a troublesome migraine, or a less pronounced septic invasion of the nervous system, because of the processes of auto-intoxication.

In the next place, make certain of the judicious adjustment of the patient's clothing about the waist, and largely its suspension from the shoulders. Corsets, in size, shape, weight, and personal fit,

are needful; certainly, more improvement in these particulars is obtainable today than in years past.

In fine, it should be impressed on the patient's mind that continued efforts on her part are ever to be made to reduce the intra-abdominal pressure from above upon the pelvic viscera and their circulation. In so doing we are instrumental and helpful in adding to woman's comfort and activity of body, as well as improving the posture, the ease, and the grace of her movements.

It has been my practice for years to direct such patients as are afflicted with an ovarian descent to assume the genupectoral position of the body, with the chest resting on the mattress of the bed (face turned of course to either side), while the pelvis is elevated to the utmost. There is no better time in the day for this duty than early in the morning after the alvine evacuation, and again in the evening before retiring. Each time should consume about twenty minutes. The patient should always avoid lying on the back; always rest in the recumbent position, on either side, somewhat semiprone.

Constitutional treatment by medicinal agents and hygienic measures are of course advantageous. Special indications arise because of anemia, debility, general nervousness, and insomnia. Prolapse of the ovary is usually detected in debilitated, sensitive, and neurasthenic conditions of the system. Always, then, endeavor to elevate the standard of the general health by all reasonable hygienic measures.

In most instances of ovarian prolapse there is more or less menstrual disorder. There is no amenorrhea, but there is some dysmenorrhea, and at times a serious menorrhagia. The menstrual flow often appears too frequently, is usually prolonged in time, as well as increased in quantity. No doubt in such cases some structural vascular lesion is induced in the endometrium, by virtue of the morbid changes in the ovary, requiring special treatment for its cure. Thus a curettement of the uterus may be done at the same sitting, preceding the abdominal section for an oöphorectomy.

There are no specifics for this affection. Naught, non-operative, can be done beyond the utilization of the aforementioned means, faithfully and skilfully employed and the use of general tonic and hygienic measures. Local means may be needed to keep the vaginal canal clean, the pelvic congestion reduced, and its circulation regulated.

Mechanical supports for ovarian prolapse, with or without any association of a backward uterine dislocation by the use of pessaries, are painful and harmful. Vaginal tampons, constructed of absorbent wool, soaked with the thymolated boro-alumino-glycerite, are better.

The latter are employed to the best advantage as follows: Not to exceed twice weekly, in the absence of the menstrual time, the

patient assumes the genupectoral posture, when gentle taxis is applied to readjust the ovary. With Sims' speculum retracting the perineum and the posterior vaginal wall the vaginal surfaces are cleaned with dry absorbent cotton, when an appropriate size and shape of wool tampon, saturated with thymolated boro-alumino-glycerite, is firmly packed into the posterior vaginal cul-de-sac, and there allowed to remain for two full days. A hot vaginal douche should follow its removal. The patient then experiences more or less comfort, from the reason that the downward movement of the displaced ovary is counteracted and mechanically supported by the wool; and the congestion is diminished by the hydrogogue action of the glycerite. Palliation may follow these procedures, so much so that further treatment may not be required.

But surgical treatment is clearly indicated in many cases because the above-mentioned means and measures properly and faithfully used, sometimes fail.

The operation of oöphorectomy may have to be done on account of some serious structural changes of the ovary. If so, it should always be done by the abdominal route, never by the vaginal method, for the reason that it can be so done more intelligently and thoroughly and just as safely. In this connection it is well demonstrated that an abdominal section affords the best of all means of determining accurately what is the condition within the pelvic cavity, the degree of the morbid process present, and what should be done for its betterment.

Modern pelvic surgery for women has unquestionably been overdone. In no way has it been so much abused as in the removal of some of the pelvic organs, under the impression that permanently good results are thus to be obtained. Experience teaches, however, in many instances the falsity of this belief. When to sacrifice the ovary is a serious question. While it is true that the removal of one ovary does not cause menstrual cessation, nor induce sterility, nevertheless it behooves us always to be careful and conservative, and to sacrifice no organ or the part of any unless reasonably necessary. With this understanding it seems to me that it should be done only for otherwise incurable structural lesions.

The abdominal section is best done with the patient in the Trendelenburg posture. The offending organ is seized by the fingers of the left hand, lifted up from the Douglas's fossa, where it had fallen, into the line of the abdominal section, when its attachments and its circulating vessels can be judiciously managed.

A needle, armed with a loop of No. 2 catgut, is first passed through the upper border of the broad ligament, adjoining the uterine wall; and a second one through the same structure on the pelvic side of the dislocated ovary. Both are firmly tied. All intermediate structures, including of course the ovary, are excised. The raw and bare surfaces remaining along these lines are stitched over

in a continuous suture and closed, to prevent bleeding and to restrain septic infection. No pain ought to supervene if the section is aseptically done.

This method of the application of the ligatures is better than with the Staffordshire knot; yes, superior in every particular, popular though the latter has been made. The Staffordshire knot implies the strangulation of an unnecessary amount of tissue; consequently, for several days following, the patient suffers needless pain.

In the making of an uncomplicated oöphorectomy the normal attachments of the diseased organ may be transfixed by a needle, armed by a loop of sterilized catgut, which, divided into two sections, may be interlocked and tied. The corresponding Fallopian tube, unless diseased, remains undisturbed.

It will be found at times that the displaced ovary is fixed and becomes irreducible, because of peritoneal adhesions, demanding then, of course, its complete extirpation. Some remnants of an old chronic pelvic peritonitis are frequently found in these cases, complicating and stubbornly resisting a complete oöphorectomy, so much so that it becomes difficult to ascertain how much of the same lies at the bottom of the patient's pelvic disease.

Before any abdominal section is commenced, conservative surgical procedures are in all cases to be entertained. A partial ovarian section, the puncturing of any distended cystic formations, may suffice. For a simple displacement, the ovary not being seriously diseased, no exsection is needed, for a suspension of the infundibuliform ligaments answers all purposes. At the time of the operation an opportunity is afforded for the best display of judgment and skill on the part of the gynecological surgeon. Of course, both ovaries are to be lifted up for inspection. Let the patient's interests always be first considered. Let her age, her social condition, her desire for future offspring, become the problems paramount for an individual solution.

There is no constant special anatomical or pathological entity always existing in these cases of ovarian prolapse, just as there are none in any forward, backward, or downward dislocations of the uterus.

Some ovaries are found comparatively healthy; some are congested or inflamed; some the seat of follicular formations; again, cystic degenerations or small abscesses may be detected. When this organ is elevated and brought into view the opportunity is also afforded to examine its appearance, determine the structural alterations within, and judiciously decide what course of action it is best to pursue. Always remove the diseased ovary entirely or in apart as indicated, but let the healthy organs remain.

All cases of ovarian prolapse are, as intimated, associated with no inconsiderable amount of constitutional depreciation of general

health. Hence, as prolapsed and tender ovaries are most pronounced in neurasthenic women, it follows that measures of a tonic and roborant kind are essential before and following any possible intervention of a surgical nature.

Whenever a complete oöphorectomy of one side is done, experiments on the lower animals (rabbits) and experiences in human females prove that the remaining healthy ovary may take on a renewed activity, so much so that in from a few months to a few years in younger women a compensatory hypertrophy of the opposite organ has recompensed for the loss.

In some of these cases, there unquestionably is a degree of distinct chronic ovaritis. The left-sided pain complained of is more continuous, persistent and severe than the right—a peculiarity no doubt attributable to the proximity of this left lateral organ to the rectum, with its scybalous masses of feces, and because of an increased congestion in the organ.

The *Faradic* electric current, judiciously administered, will be found of signal service. Its application should be derived from a very long wire, at least 1500 yards; a number 36, with a mild, smooth electric motive force, and with very rapid interruptions of the rheotome—the more rapid the better. Any increase thereof should be very slow and gradual.

The strength of this current should be regulated by the sensations of the patient; it should never be productive of any unpleasant sensations; better only barely perceptible to her. The best results follow a 15 to 20 minutes' seance.

Such an electric current is distinctly analgesic in its effects.

The *galvanic* current is adapted only to old, long-continued, chronic cases, which are probably associated with varied peri-oöphoritic morbid changes. Then, the positive pole, wrapped with moistened (salt water) cotton, is lodged within the posterior vaginal cul-de-sac, while to the negative pole is attached a flattened electrode, covered with gauze, thick in structure, wet with a potassium iodide solution, and placed over the lower abdominal surface.

The galvanic current, passed through the intermediate structures, between the two electrodes, so decomposes the potassium iodide solution, that it attracts the iodine to the positive pole, with a deposition of the alkali at the negative. In this way the alterative and resolvent influences of the iodine is promoted, perhaps better than from the use of larger quantities of the same medicament by the mouth.

It seems to me, beyond any peradventure of doubt, that electricity, in the various forms of the Faradic current and the galvanic, each scientifically employed, is a remedy of no mean power, in gynecological therapy.

There are no distinctive or fixed anatomical changes in painful or prolapsed ovaries. Most cases are noticed in neurasthenic women.

Therefore, it is by a restoration of the nervous tone of the system at large, by a roborant plan of treatment, with manifest improvement of the general health that these sensitive organs cease to be tender, although somewhat downwardly displaced. It is to better the local circulation of the blood, and to improve the nervous condition of the patient, factors largely responsible for the symptoms present, that we must direct our attention in all of our treatment, both general and local. So it is in the management of dislocations of the uterus.

I have introduced this question for two reasons: (1) it has been imperfectly dwelt upon by most authorities of gynecological literature, and (2) it is a disease of enough frequency and importance to entitle it to greater consideration on our part.

PRECOCIOUS DEVELOPMENT OF THE EXTERNAL GENITALS DUE TO HYPERNEPHROMA OF THE ADRENAL CORTEX.¹

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AND

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THE case which we present is one of those rare conditions of childhood; of unusual development of hair on the pubes and face with hypertrophy of the external genitals, without menstruation, which are apparently due to hypernephroma of one adrenal body. A similar case was presented in life at a meeting of the Philadelphia Pediatric Society in 1903 by Dr. D. J. M. Miller.² The girl died shortly afterward and the autopsy, done by Drs. C. Y. White and V. Nisbet,³ showed the growth to be hypernephroma of the right adrenal. Since the presentation of that case there have been collected by Bullock and Sequira,⁴ Guthrie and Emery,⁵ and Glynn and Dun⁶ sixteen other cases of the same type. The discussions by these authors have made this subject more clear, and have added much to the knowledge of this and allied conditions. The history of our case is as follows:

¹ Read before the Philadelphia Pediatric Society.

² Arch. Ped., 1903, p. 932.

³ Trans. Philadelphia Ped. Soc., 1904-05, V, i.

⁴ Trans. Path. Soc. London, 1905, lvi, 189.

⁵ Clin. Soc. Trans., xl, 175.

⁶ Liverpool Med. Chir. Jour., 1911, xxxi, 116.

CASE.—G. M., aged seven years, schoolgirl. Father and mother were living and well. The father was large and strong, the mother was small, frail, and suffered from splachnoptosis. One brother, two years older, was living, was rather frail, but without distinct disease. A twin sister, much smaller and of a very different temperament, was living and well. There was no family history of cardiac, renal, tubercular, or malignant disease.

The patient was the larger of the twins, weighing six pounds at birth, while the twin sister weighed four pounds. During the first summer, on bottle feeding, malnutrition, with marked emaciation and weakness, developed, and after protracted and ineffectual treatment she was taken to the seashore, where her weight increased from twelve to twenty pounds. When one year old she began to develop rapidly, and a growth of hair was noticed, first over the pubes, then in the arm-pits, then over the legs and trunk. This was attributed to the oil baths she had been receiving. The skin of the abdomen and legs was rough. She grew rapidly, and showed a surprising mental and physical development. As she began to talk it was noticed that her voice was much deeper than that of a child, and at the age of six or seven years a laryngoscopic examination showed a development of the larynx and vocal cords suggesting that of an adult man. The bass voice attracted the attention of her playmates, and as she was subjected to banter and jest, she became diffident with strangers. She proved an apt scholar, and consequently attained high grades in her school-work. She was affectionate, and preferred to play with dolls, but elected to bestow caresses rather than to receive them. Her physical development enabled her to be more than a match for her brother and sister. When three years old she would carry heavy chairs about the room with an ease that amazed her parents. Her strength was phenomenal for one of her years.

In June, 1909, when seven years old, she had chickenpox and in July, whooping cough. Previous to this time the skin of the face had been smooth and the complexion good. After this, it became coarse, red, and rough from acne, and a beard started to grow. The character of the skin of the face, and the acne and growth of hair closely resembled that so often observed in boys at puberty. There was no pigmentation of the skin. Five months later the growth of hair on the face resembled that to be found on a boy of seventeen or eighteen years. The arms and legs were muscular, and suggested a masculine development. She had never menstruated. The trunk and neck were strong and well-developed: the nipples were of the masculine type. On account of the rapid development and hirsuties, she was repeatedly examined by one of us (Jump) for affection of the adrenal glands. None was noticed, however, until about August or September, 1909, when a mass was observed (Beates) in the right hypochondriac region. This

mass grew rapidly and was painless, but in December the abdominal distention was so great that it interfered with respiration. Later a severe dyspnea developed, and on December 22, she was admitted to the Samaritan Hospital, under the care of Babcock. At this time a physical examination showed a well-developed child, fifty-three inches in height. The estimated weight was about ninety pounds. The face showed regular but not prominent features, somewhat masculine in type, with a rough, red skin, and boyish beard and moustache of a brownish color. The hair of the head was long, slightly curly, dark reddish brown in color, and of moderate coarseness.

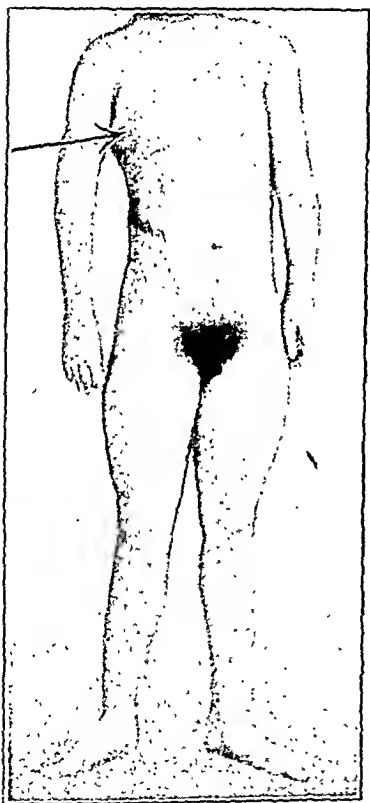


FIG. 1—G. M., aged seven years, showing development of male character.

The pubic and axillary hair was coarse, almost black in color, and the growth equalled that of an adult. The growth of hair extended from the pubic region to the umbilicus, and there was not the sharp demarcation of the upper border of the pubic hair noticed in women. A stiff growth of brownish-black hair was present upon the legs, thighs, and arms, and upon the anterior surface of the chest. The abdomen was greatly distended, especially on the right side, by a dense, elastic mass, which extended from the costal border to the pelvis. Although it was tympanitic below, it was, apparently, over the underlying colon. There was a slight enlargement of the abdominal veins of the right side, a marked linea albicans over the lower abdomen, thighs, pubes, and flanks. The left flank was somewhat distended and tympanitic. There was no increase in the splenic or hepatic dulness. The apex-beat

was in the fifth interspace, and of normal strength. The heart action was rapid (pulse, 136), but there were no murmurs. The respiration was 48 and embarrassed; there were bronchial rales, also an occasional short, unproductive cough. There was no distinct enlargement of the inguinal, axillary, cervical, or supraclavicular lymph nodes. The patient perspired freely. The voice was of a deep bass, and the child talked with difficulty on account of the dyspnea. The labia were thick and large, and there was a large growth of hair on the pubes, and a remarkable development of the clitoris; this was about one inch in length, half an inch in diameter,

and notched on the under surface, closely suggesting a hypospadiac penis. Later, after opening the abdomen, it was found that a normal infantile uterus, with ovaries and Fallopian tubes, was present. There was no evidence of a testicle in the labia or elsewhere. An examination of the blood showed the following: Hemoglobin, 85 per cent.; erythrocytes, 4,590,000; leukocytes, 8600.

The urine was negative, except for the presence of a moderate amount of albumin and amorphous urates; the specific gravity was 1030.

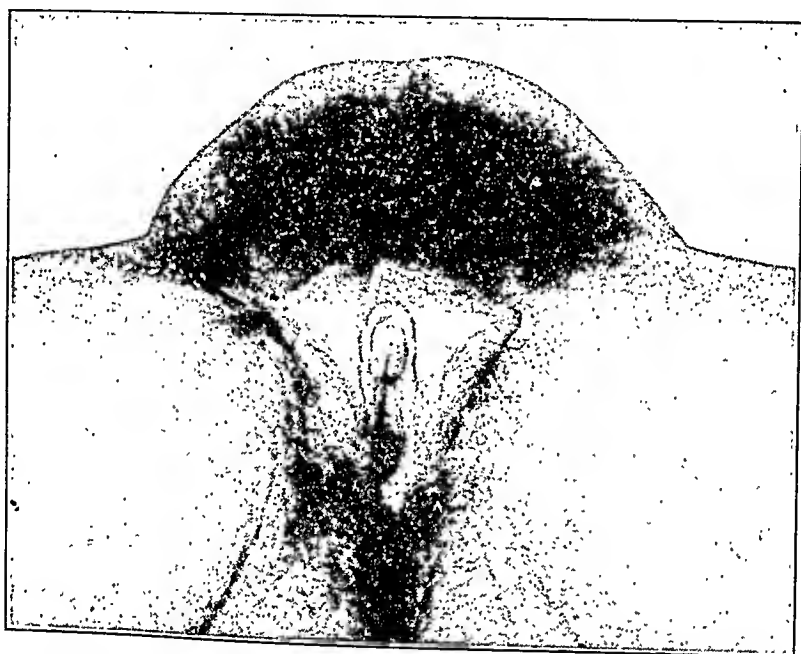


FIG. 2.—G. M., showing enlarged clitoris and growth of hair on genitalia.

The day after admission the child was etherized and a transverse incision was made over the right flank of the abdomen. This exposed an enormous perivascular and adherent hypernephroma, which was dislodged with difficulty, especially from its perivascular connections with the liver. During the operation, which lasted fifty minutes, the child became pulseless. After removing the growth the wound was closed, with drainage, and the patient stimulated, but although conscious and rational, she speedily sank, and died about three hours after the operation. The growth involved the whole of the right kidney. There was no line of separation between the adrenal and kidney. The sections which were made confirmed the diagnosis of hypernephroma of the adrenal cortex. A limited postmortem examination was made. The left kidney and adrenal were normal. The uterus and ovaries were infantile. There were no metastatic growths found in the abdomen. The pituitary body was normal.

Counting the 17 cases collected by the writers cited above, this makes 18 of such cases reported in which the presence of hypernephroma of the adrenal cortex has been proved by autopsy. There have been other cases of this character reported without autopsy, and one reported by Guthrie and Emery in which the autopsy showed both adrenals normal. The report of this autopsy was brief and the examinations evidently superficial. Of the 18 reports, 14 were girls and 4 were boys. Among these cases there occurred an overgrowth of hair on the pubes in all, on the face in 14, and in the axilla in 5; overgrowth of the body due to the fat or muscular development in all; rough skin, with acne of the face, in some; menstruation and development of the breasts occurred in but one, that of Bullock and Sequiera; pigmentation of the skin was present in many, but there was in none a distinct bronzing of the skin, as in Addison's disease. Some of them showed a mental precocity, though the majority were probably mentally dull. There is a tendency to the development of the male at the expense of the female characteristics in the girls and an intensification of the male characteristics in the boys. The occurrence of a tumor of the adrenal cortex in all of the cases is more than a coincidence, and must be counted upon as the cause of the abnormal development. Tumors involving the adrenal medulla alone are not associated with precocious development.⁷ That lesions of the adrenal cortex are associated with changes in sex characters may be shown by the following cases.

Thummin⁸ reports a case of a girl, aged sixteen years and eight months, whose menstruation began at fifteen years and ceased when she was sixteen years. She then had a moustache and beard and hair on her thorax. She grew fat and her voice became masculine. Both adrenals were the seat of tumors, designated struma suprarenalis.

Hypoplasia of the adrenals has been found in cases of retarded development of the external genitalia and in reversion to the pre-adolescent stage. Weisel⁹ reports a case of the former in a girl aged eighteen years. There were no hairs in the axilla and but few on the pubes; the breasts and external genitals were undeveloped.

Karakascheff¹⁰ reports the case of a woman, aged thirty-nine years, mother of two children, who ceased to menstruate at twenty-seven years. There was scarcely any hair on the pubes and axilla. Both suprarenals were greatly atrophied.

Glynn¹¹ says that 15 per cent. of female pseudohermaphrodites showed a hyperplasia of the cortex in both adrenals.

⁷ Glynn, *Quarterly Jour. Med.*, 1911-12, No. V.

⁸ *Berli. klin. Woch.*, 1909, No. 3.

⁹ *Virchow's Archiv.* 1904, clxxvi.

¹⁰ *Beitrage v. Zeigler*, 1904, xxxvi.

¹¹ *Quarterly Jour. Med.*, 1911-12, No. V.

How to explain the relation of hypernephroma with these signs of precocious growth is not clear. Three hypotheses may be offered: (1) The adrenal cortex and the ovaries and testicles are derived from the same embryological tissue, the Wolffian ridge. It may be supposed that disturbances in the adrenal cortex may cause changes on the analogous tissues. As opposed to this, we have the fact that in but one of the eighteen cases (that of Bullock and Sequiera) was there a development of the ovaries. The presence of hirsuties of face and pubes which have no such embryological source cannot be explained in this way; (2) that the hypernephroma of the adrenal cortex has increased its internal secretion, and this has directly, or indirectly, in its effects on other organs affected the metabolism of the body in general and of the other parts affected in particular. These have been offered by Bullock and Sequiera and Glynn to explain the phenomena. We will venture a third based on the view of Sajous:¹² (1) That the pituitary body is connected with the adrenals by direct nerve paths; (2) that it thus governs, through the adrenals, general oxidation, metabolism and nutrition. The thyroid is also a part of this system. Lesions of the adrenal cortex may then cause such changes in the sympathetic systems as will produce these particular manifestations of overgrowth. In the case of Glynn and Dun the thyroid was markedly congested and gave the impression of overactivity; the pituitary was normal. In Bullock and Sequiera's case the thyroid and parathyroids were considerably enlarged; the pituitary was not examined. In the case of Guthrie and Emery the pituitary and other ductless glands were normal. In our case the pituitary was normal and the thyroid not examined.

Our interest in these cases must be more particularly along the clinical side, with the view of finding a method for the relief of the condition. There are three groups of precocious development which could be considered: (1) Those to which we have referred above, in which there is a development of the male characters and a lessening of the female characters, which seldom show true sexual precocity. (2) True sexual maturity in young girls, characterized by pubic and axillary hirsuties, enlargement of the breasts, and menstruation. These girls do not lose any of their female characters. They are due in some cases to a growth (cyst or sarcoma) in the ovaries.¹³ (3) Early, true sexual development of boys. In some of these cases¹⁴ there have been found tumor of the testicle, of the pineal gland, or of the adrenal cortex. In the second and third groups the removal of the growth has been successfully accomplished

¹² Internal Secretions, 4th edition, vol. i, p. 80.

¹³ C. Lucas, quoted by Sequiera, Report of Society for the Study of Diseases of Children, 1902, vol. ii; Hofacker, Centralbl. f. Gynäkology, 1898, No. 41., Brohl, Centralbl. f. Gynäkology, 1897, No. 4.

¹⁴ Saechi, Riv. di Frimetria, 1895, xxi, quoted by Guthrie.

and in such there has been a reversion to the normal; the hair has fallen out, menstruation has ceased, and child-like qualities have returned. In Cushing's syndrome of overgrowth, with adiposity, due to pituitary disturbance, there is no overgrowth, of hair, and there are tardy or incomplete manifestations of the sex characters. These cases, then, need not be considered in the differential diagnosis of cause. Of the 18 cases which we have cited above, all died before they were sixteen years old. Some were operated on and died shortly afterward. In some the growth was inoperable. The symptoms of the three groups as detailed above are such as to make the diagnosis of these cases comparatively easy.

If, then, one meets a case of the first type, particularly if it be in a girl, there is presumptive evidence that there is a hypernephroma of the adrenal cortex. As there is 100 per cent. of mortality in these cases if let alone, exploratory operation, to determine if the adrenal is involved, seems advisable. If hypernephroma be found, its removal is indicated.

In considering operation on these children, we must bear in mind their apparent lack of resistance to surgical conditions. Adams's¹⁵ case lived for seventeen months after an exploratory operation showed an inoperable condition. The others which were operated on succumbed soon after the operation. Even mild surgical procedures were sometimes fatal. Ritchie's case, four years old¹⁶ died three days after an osteotomy, with no apparent cause except a slight infection of the wound. The case of O. Richards¹⁷ died shortly after tapping for the removal of the ascites. In the case of Guthrie and Emery, which showed no change in the adrenals death followed soon after the opening of a large abscess in the groin. In all of these, however, the disease was well advanced. There is but one record of a case operated on early in life, that of Dobbartin¹⁸. This child, according to her parents, was born with a tumor in the abdomen, which at operation was the size of a fist. She died shortly after its removal. As a rule, children withstand surgical operations very well, and if the operation be done as soon as the condition is recognized the chance of success seems good enough to be used.

¹⁵ Trans. Path. Soc. London, 1905, lvi.

¹⁷ Guy's Hosp. Rep., lix.

¹⁶ Cited by Bullock and Sequiera.

¹⁸ Beiträge z. pathol. Anat., 1900, xxviii.

SYMPTOMS SUGGESTING PITUITARY DISORDER.¹

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REMARKS about the pituitary and other organs of internal secretion need preliminary explanations as to the writer's attitude. I realize the ease with which a group of systematized delusions may be built about the functions of the adrenal, thyroid, pituitary, or all of them together, but can see no evidence for a paranoid condition in the works of Cushing, Ashner, Biedl, and others where facts are presented and inferences drawn in a way which robs the skeptical and indifferent of the excuse that these affairs are too mysterious for the every-day work of the clinician. It has long been the proud boast of the general hospital pathologist that he knew nothing of the brain; a somewhat similar attitude is found in the psychiatrist's pride in being able to overlook all the confusing symptoms of internal secretory disorder, except that non-incriminating group found in Graves' disease.

Single cases of polyglandular and hypophyseal disease are reported in profusion. As best illustrated in Dr. Cushing's book, it is not hard to find descriptions of mental symptoms in a series of pituitary cases. I cannot, however, find pituitary symptoms described in a series of mental cases, or in a given population selected for their insanity, and this is the excuse for this paper, a survey which makes no pretence in intensive study of any particular case.

The problem of doing something to establish the frequency of pituitary symptoms in the Danvers population naturally divided itself into two parts, (1) the frequency of pituitary lesion in consecutive autopsies, and (2) the frequency of pituitary symptoms in the patients now in the hospital.

Approach to the first problem was easy. An autopsy index card was found which listed 45 lesions, 3 of them tumor with acromegaly; 4, tumor without acromegaly; 3, tumor secondary to other foci; and several instances of enlargement, cysts, marked adhesions, etc.

With the abundant evidence of the widespread results of certain lesions of the pituitary, it is worth noting that the pathologist had his attention called to obvious evidences of disease in 45 cases, or to 1 in 33 of 1600 consecutive insane patients—and this in routine autopsies from 1879 to 1912, where many glands escaped any sectioning for the microscope, and even those prepared for the microscope were removed and stained by a method which showed practically nothing of their functional ability, but allowed only a gross measure of a gross damage.

¹ Read at the March, 1913, meeting of the New England Society for Psychiatry, Howard, Rhode Island.

One of these cases was described by Dr. Worcester in 1896.¹ Another, clinically, was a picture of myxedema; autopsy disclosed a tumor filling the sella turcica. I give one other case to show a less definite symptom group: Last summer a married woman entered the hospital, emaciated, cyanotic, with a pulse that at one time was 174 to the minute, at other times 80, with glycosuria, silky infantile hair on scalp, eyebrows, and body, with clubbed fingers and thick, brittle nails, sluggish and irregular pupils, a slight increase in deep reflexes, and a negative Wassermann. Though the adrenal was supposed to be at fault, autopsy showed, beside adrenals with many cells missing, cystic ovary, atrophic breasts, a very large injected pituitary crowded with the nuclei of new cells.

To get some idea of the incidence of symptoms suggesting pituitary disease in the patients now in the hospital, wards were visited once with the physician in charge, about 950 patients coming in for a hasty observation, which was verified by a reference to the symptoms already recorded in the histories. Cushing's

four groups of symptoms were kept in mind: (I) general pressure symptoms; (II) neighborhood symptoms, including visual and nasopharyngeal disturbances and uncinat epilepsy; (III) glandular manifestations, including skeletal over- and undergrowths, cutaneous and the important hair changes, adiposity, altered carbohydrate tolerance, polyuria, drowsiness, epilepsy again; (IV) symptoms referable to other ductless glands, including infantilism, pigmentation, persistent thymus. In this way ten cases were upturned whose symptoms, as recorded in the histories in the routine way, suggested a pituitary involvement.

CASE I.—A single woman, aged fifty-two years, who had scarlet fever at five years and had been feeble-minded since. She showed facial asymmetry; thyroid apparently diminished; poor hearing, poor vision, drowsiness, exophthalmos, a Wassermann positive on the serum, but negative on the cerebrospinal fluid; adiposity; height, 4 feet 10 inches; weight, 150 pounds.

CASE II.—Married woman, aged forty-five years. At thirty years her eyesight began to fail, and at present she has cataracts



FIG. 1.—Case II.

¹ Boston Med. and Surg. Jour., April 23, 1896.

which do not allow the condition beneath them to be estimated. At thirty-seven years, with the menopause, she began to get more fleshy, had frontal headache, which was much increased by noise, and severe bleeding from the nose. Height, 4 feet 10 inches; weight, 199 pounds. Her face was broad, nose short, vertex flattened; hands and fingers were short and thick; Wassermann was negative (Fig. 1).

CASE III.—Single woman, aged thirty-six years, who had meningitis at three and a half months, followed by hydrocephalus and feeble-mindedness. The circumference of head was $62\frac{1}{2}$ cm.; height, 4 feet 8 inches; weight, 172 pounds; body square, covered with a deep fatty panniculus; arms short; Babinski present on both sides. The knee-jerks were very active. The patient was drowsy at times. She showed an irregular disk on both sides; veins dilated; arteries much smaller.

CASE IV.—Single woman, aged forty-one years. Imbecile, who as a girl had considerable headache and dizziness. Underdeveloped; overnourished; hydrocephalic; sluggish pupils; exophthalmos.

CASE V.—Girl, aged sixteen years. Height, 4 feet 9 inches. Weight, 100 pounds; fatty panniculus; hair fairly abundant; convergent strabismus; nystagmus. The left optic disk showed a nasal pallor.

CASE VI.—Married woman, aged twenty-three years. Always indifferent and feeble-minded. At nineteen years she had periods of stiffening, when she became cold, pale, with lips blue. Her height was 4 feet 7 inches; weight, 78 pounds on admission, and after typhoid at twenty-one years her weight was 98 pounds. In this patient was shown the body of a well-developed fat woman with the thin face and neck of a child.

CASE VII.—A man, aged fifty-one years. Since a fright at the Chelsea fire, when he was forty-six years, he has had many convulsions, preceded by a bad taste in his mouth. On entrance the skin of the forearms and abdomen was dry and scaly. Wassermann test was negative throughout; there was sugar in his urine for the first week. With a history of diminished taste for the last two years, there was an utter failure to pass the routine test for smell.

CASE VIII.—A widower, aged fifty-five years, who at twenty years received an injury to his back. At fifty-four years he was annoyed by falling to sleep at meals, in street cars, in conversation. Apparently normal mentally, he went to the Hot Springs to get relief from this condition, and in seven weeks was brought back violently insane. For some months, at the McLean Hospital, he was noisy, jocose, flighty, and distractible. This mental condition continued at the hospital, and he showed in addition a striking sexual complex full of symbolisms. His external genitals

approached the infantile type, and he had a tendency to a feminine distribution of hair. His height was 5 feet 7 inches. In the last year he had gained 22 pounds; weight, 229 pounds. He would fall asleep frequently, often in awkward positions. He was drowsy and manic by turns each day (Fig. 2).

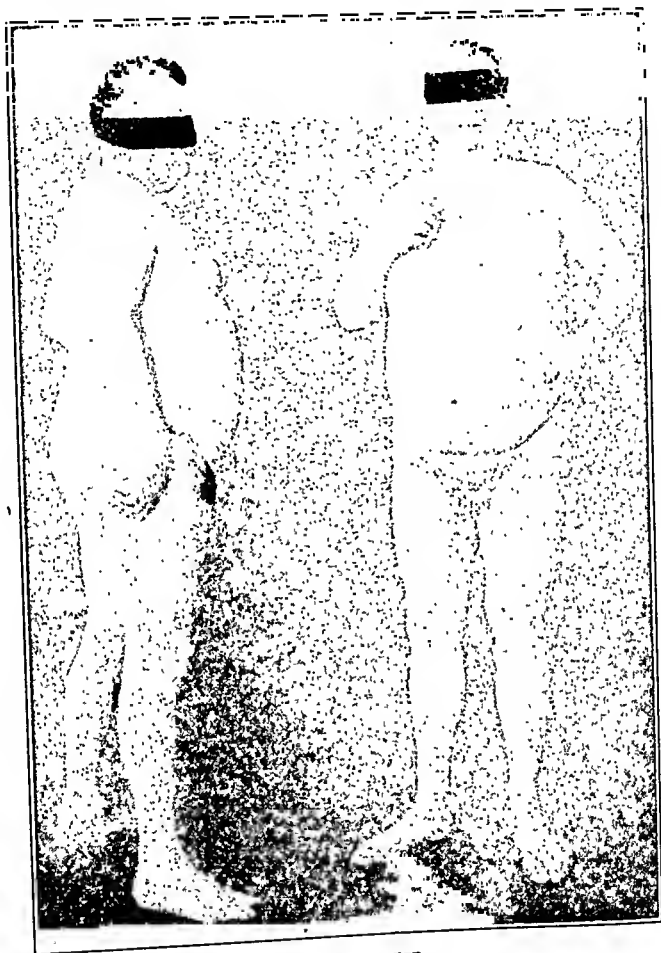


FIG. 2.—Case VIII.

CASE IX.—A single woman, aged thirty-seven years, always feeble-minded. She was formerly considered pretty, but her face had changed. She was round-shouldered; the hands, femurs, and ears were of unusual length.

CASE X.—A single woman, aged twenty-three years; 5 feet tall; weight, 232 pounds, lack of axillary and pubic hair; infantile external genitalia.

Intensive study of these cases would probably remove some of them from consideration, but, on the other hand, applied to the whole hospital population, special methods would probably add many more cases to the list.

My point is this: State hospital populations, because of their long average residence, possibly because they are selected as insane, and because they do not in the first instance come to a surgeon seeking relief from the pressure symptoms, offer unusual opportunities for surveys of the incidence of pituitary symptoms to balance the intensive studies of the surgeon and experimentalist. For this more superficial work special methods of diagnosis are relatively unimportant; good routine physical examinations are wanted. Nothing better illustrates the value of the conscientious physical record than a glance at histories from a polyglandular viewpoint, and happily nothing so alleviates the tedium of what is often regarded as a useless task as the realization of inter-relationships which give life and color to an otherwise bald and uninteresting statement of facts.

THE VALUE OF AUTO-INOCULATION IN PULMONARY TUBERCULOSIS.¹

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DR. MARCUS PATTERSON, of Frimley, claims to influence the course of pulmonary tuberculosis favorably by "auto-inoculations" induced by labor. He states that even "severe" auto-inoculations, if controlled by immobilization, benefit the patients. He considers that "the aim should be to increase the patient's labor—insofar as is consistent with his physical capacity—in order to produce a marked deviation in the temperature on one or another of the grades, and finally enable him to do five hours hard outdoor work with little deviation." To collect evidence which shall help us to judge the value of such auto-inoculations is the object of this paper.

That graduated exercise has great value in attaining health and in preparing the body for athletic contests or work was well known to the ancients. Brehmer recommended exercise for consumptives. Walther prescribed graduated walking exercises for his patients for many years at Nordrach. Graduated labor as a therapeutic measure seems to have been first applied systematically to consumptives in sanatoria by Dr. Lawrence F. Flick. Great credit for elaboration of the system and popularizing it, for calling attention to the symptoms of slight "auto-inoculations," and the importance of treating them is due to Dr. Patterson.

¹ Read before the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 8, 1913.

While unrecognized auto-inoculations may, of course, occur without rise of temperature or other symptoms, yet the most important single symptom of auto-inoculation and the one chiefly relied on for this study was a rise of temperature above 99° . Patterson considers even 99° , with headache, loss of appetite, or other marked constitutional symptoms, reliable evidence of auto-inoculation in men and 99.6° in women. Many tuberculous women are subject to a rise of a few tenths of a degree during menstruation, but at other times I have not found so marked a difference between men and women.

While it may be admitted that a temperature of 99° in some individuals does, and that 99.2° or even 99.4° in other individuals does not, usually mean tuberculous toxemia, yet it was considered the safest guide for this work.

Shortly after the opening of the institution it became our routine practice to interview patients with temperature over 99.5° and record the complications on the temperature charts. All complications causing fever were therefore eliminated with reasonable accuracy. The material at hand consisted of the records of 1517 patients discharged from the Rhode Island State Sanatorium during the years 1906 to 1911 inclusive. All far-advanced cases and all moderately advanced cases whose temperatures were not reduced absolutely to normal for periods of two or three weeks were eliminated. All tuberculin-treated patients, all children, and likewise all colored persons, have been excluded as not forming a fair basis of deduction. In the following table the remaining 746 patients have been classified according to the average frequency of the fever days in the left-hand column, and according to their present condition in the remaining columns. The majority of these auto-inoculations were between 99° and 99.6° , and for one or two consecutive days only, but a small minority had long runs of fever.

TABLE I.—End Results Classified According to the Average Frequency of Fever Days.

Average frequency of temperature.	Well.	Living and working.	Living.	Dead.	Totals.	Per cent. Dead.
3 times week	12	9	8	50	79	63
2 times week	30	20	25	69	114	47
Once in 1 week	62	39	30	74	205	36
" " 2 weeks	34	21	14	33	102	32
" " 3 weeks	22	16	14	14	66	21
" " 4 weeks	16	16	11	14	57	23
" " 2 months	12	9	6	5	32	15
" " 3 months	6	6	4	1	17	5
" " 6 months	10	..	2	..	12	0
Never	10	12	5	5	32	15
Totals	214	148	119	265	746	35

From the above table it appears that both the recovery and the mortality rate of tuberculous patients bear a pretty constant relation to the number of auto-inoculations as determined by the number of fever days. Everyone would expect that patients who had some fever with an average frequency of three, two, or even one day in a week would turn out badly. But if occasional auto-inoculations evidenced by slight fever are beneficial, should not those who have auto-inoculation on an average of one day in two, three, or four weeks do better than those who have them one day in two, three, or six months, or none at all?

The great majority of the 93 patients whose fever days averaged one day in two months or more of residence had only a slight initial fever for a few days after admission, so that they had no inoculations which would be considered of therapeutic value by Patterson, and yet these are the patients whose recovery best stood the test of time.

Our patients are kept in bed with a temperature of 100° or over if persistent, and for anything above 99° in the morning; but as we have not carried out the complete immobilization described by Patterson, it may be said that some of the patients not receiving this complete immobilization were injured by these auto-inoculations which otherwise might have benefited them. To ascertain whether lack of control of the immobilizations could have affected the result, and also to eliminate from consideration the worst types of cases, all patients whose temperatures were not always reduced to 99° or below in less than one week were excluded from the following tabulation:

TABLE II.—End Results Classified According to the Average Frequency of Fever Days. All Auto-inoculations Controlled in Less than a Week.

Frequency of fever.	Well.	Living and working.	Living.	Dead.	Total.	Per cent. Dead.
2 times week	3	3	2	6	14	42
Once in 1 week	20	14	9	17	60	28
.. 2 weeks	24	12	12	18	66	27
.. 3 weeks	17	13	11	14	55	25
.. 4 weeks	14	14	12	10	50	20
.. 2 months	13	9	6	6	34	14
.. 3 months	5	6	3	1	15	6
.. 6 months	9	0	2	0	11	0
Never	9	13	5	5	32	15
Totals	114	84	62	77	337	22

That the results in patients who had no reactions were not quite so good as those who averaged one auto-inoculation in six months, may fairly be explained by the fact that the former had an average residence of only 2.8 months against 6.5 months for the latter.

The principle that the fewer the fever reactions the more permanent the results is clearly seen in Table II, which also shows

that the poor results in those having auto-inoculations was not due to lack of prompt control.

All our patients had been on a system of graduated exercise and work about the institution since the fall of 1905. The system is similar to Dr. Patterson's except that there has been no so-called "complete immobilization" and no graduation of labor in foot pounds, and that in our application of graduated labor we have been trying to avoid instead of trying to induce temperature reactions. In order to be discharged "disease arrested," our classification requires that there must have been no hemoptysis, acute pleurisy, troublesome cough, nor fever temperature over 99° for at least two months, the weight, strength, etc., being restored to normal. Tubercle bacilli may or may not be present. The majority of our patients discharged with their disease arrested have been worked up to four or four and one-half hours labor, such as sweeping, scrubbing, and waiting on table, in addition to three or four hours' walking exercise, but a few have not done quite so much. In order to make a more searching inquiry as to the value of auto-inoculations under graduated labor, the records of 169 patients who were classified as "disease arrested" on discharge have been tabulated in two classes: (1) Those who were either afebrile throughout the entire period of sanatorium residence or whose slight fever subsided in a week or two after admission and afterward remained afebrile, and (2) those who had occasional auto-inoculations over a considerable period, but whose temperature finally settled absolutely to normal for over a month before discharge. In most cases this period of normal was at least six or eight weeks. Patterson's rule of ignoring an occasional rise of temperature in women provided it kept under 99.6° and was unaccompanied by constitutional symptoms was followed. A few who had a single rise to 99.5° or less were allowed in Class 1. No patients were admitted to Class 2 unless they had at least three auto-inoculations, and the majority had from three to six. Patients in Class 1 had their disease arrested without auto-inoculations, as indicated by fever, and those in Class 2 had their disease arrested after a period during which they had occasional auto-inoculations, as evidenced by fever.

The present condition of these patients is shown in the following table:

TABLE III.

	Well.	Living and working.	Living.	Dead.	Total.	Per cent. Dead.
Class 1, without auto- inoculations	28	18	10	9	65	13.8
Class 2, with auto-inocu- lations	39	31	13	21	104	20.2
Total	67	49	23	30	169	

While pulmonary tuberculosis is progressing favorably toward arrest, the value of graduated labor in restoring the normal muscular tone in working people, provided it can be done without inducing symptoms, can hardly be denied. There is some risk that fever reactions may be induced no matter how much we try to avoid them, but this risk must obviously be taken sometime if the patients' usefulness is ever to be restored. Graduated labor has value as a test for the patients' fitness to return to work, and also as a means of avoiding the injury to intellect and morals resulting from long continued idleness. However attractive the theory may be that fever reactions induced by labor have a curative value in pulmonary tuberculosis it cannot be accepted until proved by comparing the subsequent histories of patients who have had such reactions with similar patients who have not had them.

SUMMARY. 1. The fewer the fever days in pulmonary tuberculosis the better the chance of recovery.

2. Patients who have had no auto-inoculations evidenced by fever during sanatorium residence have a very high recovery rate.

3. Patients who finally achieve a stable temperature after a period of occasional auto-inoculations do not avoid relapse so successfully as those who obtain arrest without such period of auto-inoculations.

4. It should be our aim to avoid rather than to induce fever reactions, or auto-inoculations, in pulmonary tuberculosis.

THE EARLY SYMPTOMATOLOGY OF CANCER OF THE ESOPHAGUS.

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DURING the past two years the writer has had occasion to examine a considerable number of patients having cancer of the esophagus, and has been impressed with the difficulty which is experienced by the profession in recognizing the early symptoms of this disease. Aside from any practical reasons relative to a safe operative treatment of cancer of the esophagus, the mere desirability of knowing at the start the real condition of any patient should be sufficient reason for making an early diagnosis. In other words, to aim to make the earliest possible diagnosis of any pathological condition is but a part of the perfecting of medical science, and, even if the condition may be at present incurable, we should rather

feel the more stimulated to achieve its early recognition as the direct step toward the discovery of an ultimate cure.

At the present time, some of the problems connected with the successful removal of epithelioma of the esophagus have not been answered. We are, however, near their solution; how near is demonstrated by the fact that the resection of the esophagus has been shown to be technically possible upon man, and is already an easily accomplished procedure upon the dog.¹ In the writer's opinion it is not too much to expect that at the present time the resection of the carcinomatous esophagus could be an accomplished fact upon the human being by the technique described by him² were opportunity offered to perform this operation under favorable conditions.

Every effort should, therefore, be exerted toward finding these patients in the earliest stages of their disease. By this is meant not only the necessity of employing some exact objective method of diagnosis, but also the necessity of suspecting possible esophageal cancers in their incipency.

With esophagoscopy we have at our command objective methods of arriving at an exact diagnosis. By these means, especially the latter, nothing can be simpler than the making of a correct diagnosis of esophageal affections once their presence is suspected. Not only can the presence of a cancer and its exact location be determined, but also by the removal of a small piece for microscopic examination the degree of malignancy. Furthermore, in case the growth is situated at the lower extremity of the esophagus it can be ascertained whether it originated within the stomach or esophagus. This fact may not seem to be a matter of much clinical importance, but, if operative removal is considered, it becomes a consideration of much importance, for it furnishes a basis for estimating the probable size of the growth.

With, therefore, such an accurate method of diagnosis at our disposal, the early recognition of cancer of the esophagus resolves itself into a correct appreciation of its earliest symptoms. In other words, we have at hand means to make the diagnosis without error the hour the trouble is suspected, and the only bar to our actually doing so in an early stage is our difficulty in suspecting the trouble in its beginning.

The writer is convinced that the existence of cancer of the esophagus is suspected later than it should be, and that errors of diagnosis, even up to a late stage in the disease, are more frequent than it is generally supposed. Richard Cabot makes the statement in his recent paper upon diagnostic errors, among 3000 cases coming to autopsy, that a greater proportion of mistakes were made in the

¹ During the time in which this paper was in press, the reports of two cases of successful resection of cancer of the esophagus have been published.

² *Annals of Surgery*, July, 1910.

diagnosis of cancer of the esophagus than in any other condition. Out of 20 cases, 4 were missed altogether and 3 others merely suspected during life. He further states that the percentage of incorrect diagnoses would have been larger but for the routine use of the esophagoscope. He did not refer to cancer of the esophagus in the early stages, but to failures to recognize the true condition during life.



Cancer of esophagus, showing at (x) section across abscess cavity in lung and pleura.

The accompanying photograph represents a cancer of the esophagus which was diagnosed as empyema until the autopsy revealed the real cause of death. For this specimen I am indebted to Dr. Larkin, pathologist of the City Hospital. An early perforation of the growth had taken place, with an encapsulation of pus within the lung and adjacent pleura.

In my own experience the mistakes in the early diagnosis of those cases of cancer of the esophagus which have been submitted to me for an esophagoscopic diagnosis have not been very frequent.

Only 4 out of 21 cases have been suspected during the first two

months of symptoms. Rarely is a patient sent for esophagoscopy before four months from the date of his first symptoms, and several cases have not been examined until eight months to one year from the date of the first symptom. If cancer of the esophagus were a curable condition, such delay would be inexcusable. There is a general and well-recognized apathy toward the early recognition of cancer. Experience with cancer of the stomach where we have to deal with a lesion susceptible to radical removal, but where success is almost universally prevented by delayed diagnosis forces us to believe that the delay in the diagnosis of cancer of the esophagus is to be attributed in large part to indifference. Furthermore, cancer of the esophagus is a comparatively infrequent lesion. Probably not more than 1200 originate yearly in the United States; this figure is based upon the percentages of esophageal cancers to the total number of cancers. Not many physicians, therefore, see these cases. For this reason, there is a general ignorance concerning the early history and a general failure to recognize the necessity of applying absolute methods of diagnosis upon the appearance of the first symptoms. Whatever form of treatment may be applied to cancer, success cannot be hoped for unless an early diagnosis is made.

With, therefore, the yearly increase in our knowledge, resulting from research work upon intrathoracic conditions, it is not too much to hope that what has already been regularly accomplished upon animals, and what has been proved to be possible upon human beings, may yet be safely performed upon the latter—namely, the resection of the esophagus. In connection with any treatment, however, particularly in connection with the operative treatment, the question naturally suggests itself. How early may cancer of the esophagus be recognized if it is looked for upon the first appearance of symptoms? Autopsy statistics furnish strong evidence that it may be recognized when still of comparatively small size and limited to a short segment of the tube. At least 50 per cent. of the patients die without metastases.

These observations are further confirmed by the findings upon the operating table. The writer will limit himself entirely to his own experience: He has operated upon four patients with cancer of the thoracic portion of the esophagus. Although a radical operation was undertaken in only one of these cases, none of them was really inoperable. Enlarged glands were, however, present in all. The operation was undertaken in the four cases at four months, three months, eight months, and again, eight months from the date of the first symptom. The impression was very strong that had the patients been objectively examined in the beginning, favorable conditions for resection would have been found.

What, then, are the first symptoms of cancer of the esophagus? It is usually considered that dysphagia is the earliest symptom.

Such is often the case, but it is not generally appreciated that the dysphagia may be at first only temporary. This often has been the case among patients who have been referred to me. The dysphagia has entirely disappeared for a considerable length of time before it became permanent. In four of Cabot's 20 cases there was no dysphagia throughout the disease; I have not met with such a large proportion of strictly esophageal cancers in which dysphagia has been entirely lacking. An absence of dysphagia occurs more frequently in patients whose lesion has begun in the cardiac end of the stomach, involving the esophagus later. These patients have not been included in the present series. It is true, however, that dysphagia is long absent with true esophageal cancer. One patient during the first six months had three or four attacks of only a temporary dysphagia. In other patients the dysphagia at first may amount to a brief choking sensation only. It is not always the first symptom. Instead of it there may be some definite new abnormal sensations referable to the throat and interior of the thorax or region beneath the xiphoid cartilage. One patient referred to me complained of a sticking sensation in the throat and supposed that she had swallowed a tooth-brush bristle. An examination for such a cause of her trouble within the pharynx was actually made, and her physician assured her that there was nothing the matter. The patient still felt the disagreeable sensation, and returned after four months, with increased trouble. Six months after the beginning of her affliction the writer examined her and easily removed from her esophagus a small portion of a squamous-celled epithelioma for microscopic diagnosis. In other patients the new abnormal sensation may be described as a sense of pressure, or a dull, constantly recurring discomfort, or in still others, an actual pain. Patients complaining of such symptoms, which are possibly referable to the esophagus or stomach, should not be discharged as neurasthenics, but should be urged to have an esophagoscopy examination. The writer has not met with a large number of strictly esophageal cancers in which dysphagia has been entirely lacking; an absence of dysphagia occurs as already noted more frequently in patients whose lesion has begun in the cardiac end of the stomach, involving the esophagus later. These patients have not been included in the present series.

In other patients the first symptom has been a cough or increase in the amount of mucus in the throat; in others, anorexia has been the first symptom.

The accompanying table gives the first symptom of 21 patients whom the writer has recently examined, and of whom he has kept a more accurate record than in the early period of this study.

The table also gives the time after the development of the first symptom at which an attempt was made to settle the diagnosis definitely.

A review of the table makes it quite clear that an earlier diagnosis was easily possible in all of these patients. In most of them the true nature of the dysphagia was misunderstood, and in a small minority only was the diagnosis made before three to four months after the patient had symptoms. When we consider that the total duration of cancer of the esophagus is probably about two years, and that few patients live longer than twelve to fourteen months from the date of their first symptoms, a delay of three or four months means a delay of a considerable proportion of the total duration of the disease.

The writer, of course, realizes that even from well-informed quarters the question will be asked, "Of what use is an early diagnosis of cancer of the esophagus." The toleration of such a *laissez faire* attitude stultifies research and is equivalent to the denial of the possibility of any further therapeutic progress.

In conclusion then the purpose of this paper is to emphasize the obligation resting upon the profession to study more carefully the early symptomatology of cancer of the esophagus, and to urge the immediate objective examination of patients suffering from symptoms which may even remotely be referable to the esophagus.

No.	Patient.	First symptom.	Subsequent early symptoms	Time intervening between appearance of symptom and the making of diagnosis.
1	Bu.	Pain beneath xiphoid.	Dysphagia began two weeks later.	3 months.
2	Do.	Attacks of temporary dysphagia.	Continuous dysphagia four months later.	9 months.
3	Flo.	Dysphagia.	Masked by symptoms of appendicitis. After the appendix was removed the esophageal cancer was discovered.	2 months.
4	Ab.	Dysphagia.		6 months.
5	Na.	Pain and dysphagia.	Severe pain.	2 months.
6	St.	Increase of mucus in throat; pain on left costal border.	Loss of strength; dysphagia six months later.	7 months.
7	We.	Sudden attacks of temporary dysphagia.	Several similar attacks during next nine months, then constant dysphagia.	11 months.
8	Lo.	Dysphagia.	Constant dysphagia and vomiting.	3 months.
9	Kr.	Dysphagia.		3 months.
10	Mey.	Dysphagia.	Constant vomiting after nine months.	6 months.
11	Mc.	Tickling in throat.	Frequent vomiting and dysphagia after four months.	6 months.
12	Ma.	Dysphagia.	Vomiting and increase of dysphagia.	6 months.
13	Se.	Dysphagia.		5 weeks.
14	Bl.	Dysphagia.		3 months.
15	Sh.	Anorexia.		2 months.
16	Ja.	Dysphagia and constant dull pain over lower end of sternum.	Dysphagia one month later.	4 to 6 months.
17	Le.	Dysphagia.		3 months.
18	Su.	Dysphagia.		1 year.
19	W.	Tickling in throat.		6 months.
20	F.	Anorexia.		7 months.
21	E.	Temporary dysphagia.	Dysphagia and pain. Constant dysphagia after two months.	7 months.

REVIEWS

ANATOMY AND PHYSIOLOGY. A TEXT-BOOK FOR NURSES. By JOHN F. LITTLE, M. D., Assistant Demonstrator of Anatomy, Jefferson Medical College. Pp. 483 with 149 engravings and 4 plates. Phila. and New York: Lea & Febiger, 1914.

THE present volume, one of the Nurses Text-book Series, is fully up to the standard of these popular and practical books. The author has taken the two great subjects of anatomy and physiology and has so carefully correlated them that the reader, while learning about the anatomy of the body, at the same time learns the function of that part; surely a most facile and interesting method of acquiring knowledge. The relation of these two great subjects has been well maintained though at times it seems as if too great stress had been laid upon anatomy, with the neglect of the equally important physiology. Certainly in considering the relative importance of the two subjects to nurses, it would be advisable to subordinate the question of what the body is, to what the body does. Excepting this criticism and criticism of some of the theories of physiology as expressed by the author, the remainder of the book is most praiseworthy. There is a careful condensation and clear expression of the subject matter, two extremely important and most difficult factors in the process of bringing large comprehensive subjects down to the level of the beginner who is to be taught only the bare elements of the subject.

Those who have to do with the training of nurses realize the inadequacy of many of the existing so-called nurses' text-books. They should be the first, therefore, to welcome a practical yet carefully and accurately prepared book such as this and will doubtless lend their enthusiastic support to the effort that is now being made to produce books that are suitable to the needs of the training school.

J. H. M., JR.

BLOOD PRESSURE FROM THE CLINICAL STANDPOINT. By FRANCIS ASHLEY FAUGHT, M.D., Medico-Chirurgical College, Philadelphia. Pp. 281; illustrated. Philadelphia and London: W. B. Saunders & Co., 1913.

WRITTEN by a man who has devoted considerable time and study to the clinical aspects of blood pressure, this hand-book, an ampli-

fication of his pamphlet on the sphygmomanometer (published in 1909), presents a *resume* of the clinical and experimental work, which has developed so largely the usefulness and popularity of this test.

Except for Janeway's book on the "Clinical Study of Blood Pressure" (published in 1904), there has been no noteworthy addition in book form to the rapidly accumulating stock of knowledge on the subject of sphygmomanometry. The appearance, therefore, of such a book is timely, and it should prove useful. Following Janeway's method, the first part of the book, and in the reviewer's opinion the better part, deals chiefly with the mechanical and physiological principles of sphygmomanometry. In the latter part an attempt is made to consider from the clinical viewpoint of etiology, pathology, diagnosis and treatment, the different diseases in which a knowledge of the blood pressure is of importance. Its small size necessarily precludes thorough consideration of all these branches. It would seem better either to have encroached on the field of medical text-books with a larger book or to have restricted the discussion to those features directly concerned with blood pressure. Chapter two includes an interesting historical review with a description of the different types of sphygmomanometers invented. It is a pity that although the author's two instruments are described and illustrated in some detail, the Nicholson adaptation, considered by many to be the best on the market, is not even mentioned.

It is also regrettable that in a book on such a timely and interesting subject so many misprints and errors of spelling, punctuation, and grammar should be found. For instance, on page 17 is found "bacterial" for arterial; page 114, "subtil" for subtle; page 134, "mellititis" for mellitus; page 141, "phenomiæ" for phenomena, and "grandular" twice for granular; page 162, "antidates" for antedates; page 163, "percordial" for precordial; page 232, "nitrate" for nitrite. Clearness might be helped in many places by a more liberal use of commas, also by properly punctuating the end of a quotation (page 91).

Numerous footnote references throughout the book afford ready access to the original authorities. Again, however, the form is open to criticism. Instead of following the regular method of giving year, volume, and page, one or other of these items is nearly always omitted and in some important citations the reference is not given at all (page 124). The matter dealt with at the head of page 221 is the same and in the same words as on page 62.

Paper, illustrations, and type are all satisfactory, though the headings are occasionally not typed consistently (*e. g.* Graupner's and Shapiro's test, page 164; "Other Infections," page 109, etc.).

The presentation of facts is for the most part excellent. The last two chapters on methods of controlling blood pressure should

prove especially useful. One might take exception however, to the statement that "strophanthus has proved unreliable and should not be used" in the treatment of myocardial degeneration (page 166). Still more strenuously do we disagree with the opinion that "thus far no accurate means of measuring the several factors (of the heart's function, *i. e.*, rhythmicity, irritability, conductivity, etc.) has yet been found." Instead of thinking that "the many methods which have been suggested from time to time, all fall short of any great degree of accuracy," we hold that the increased scientific accuracy in measuring many of these very factors has led to the greatest advance in our knowledge of heart disease for at least the past quarter century.

E. B. K.

HYGIENE OF SANITATION. A TEXT-BOOK FOR NURSES. By GEORGE M. PRICE, M. D. Pp. 236. Philadelphia: Lea & Febiger, 1913.

THE author states in his preface that this book is an attempt to give to the nurse a knowledge of the elements of hygiene in its various branches. He might well have made this statement more comprehensive, for the book, written in elementary manner, could be readily comprehended by the layman and read with much profit. It contains masses of information that could be used every day by those interested in the proper hygiene of the home, of the person, of the school, of the food supply, or of the various occupations. The author has made the apparent scope of his book too small; he might well have broadened it and dedicated the book to the general public. It is one of the few text-books intended for nurses that adequately meets the requirements and should prove a welcome aid to those in charge of the instruction of nurses.

J. H. M., JR.

THE PRACTITIONER'S ENCYCLOPEDIA OF MEDICINE AND SURGERY IN ALL THEIR BRANCHES. By J. KEOGH MURPHY, M.C. (Cantab.), F.R.C.S. Pp. 1423; London: Henry Frowde, Oxford University Press.

AN encyclopedia of this kind, coming as it does between the brief medical and surgical summaries on the one hand and the systems of medicine and surgery on the other, is well conceived. It is surprising that in the comparatively brief compass of some 1400 pages such a multitude of subjects has been so satisfactorily covered.

It is presented as a book for the general practitioner who in his work is called upon to give advice in conditions which, in the course of years, will cover the whole domain of medicine and surgery. For the physician whose lot falls away from the medical centres this book will prove an especial boon and will in part compensate him for the lack of broadening and stimulating influence of the general and special medical societies, with their ready access to medical libraries and current medical literature.

The division of the matter into the main headings of medicine, surgery, eye, ear, nose, throat, and skin, is a natural one and much more acceptable for general and special reading than the oft used alphabetical arrangement.

As an actual working tool, in the hands of a practitioner who has no further access to medical knowledge, it has suffered from the necessary condensation imposed on the writers.

As a general medical educator, this book should prove invaluable in the hands of those who might otherwise fail to keep abreast of the landmarks in medical progress. It also offers to the practitioner an opportunity to keep his general knowledge in a well rounded form.

A. A. H.

WHAT HEART PATIENTS SHOULD KNOW AND DO. By JAMES HENRY HONAN, M.D., Special Lecturer on Cardio-vascular Disease in the Univ. of Georgia, etc.; pp. 204. New York: Dodd, Mead & Co., 1913.

THE object of this book, in the words of the author's preface, is to give encouragement and hope to those who know they have heart trouble, to urge those who are suspicious of its presence, to seek advice in time; to help, if possible, both these classes of persons to make the most of their lives with the limitations which deviation from the normal imposes. To this end the first half of volume, and to the reviewer's mind much the more valuable half, is devoted to hygienic considerations, adapted especially to heart patients, under such capitals as relaxation, clothing, exercise, diet, sleep, etc. In the latter half, having presumably obtained the interest of the reader, the dryer and more technical anatomical and pathological details are considered. Emphasis is laid throughout on the fact that "this book is in no sense to be a substitute for the physician, nor a promise of health to all who read its pages."

The advisability of offering such a book to the lay public is in itself open to criticism.

Given the need for such advice in printed form, the recommendations are excellent.

Objection might be taken to a few details: the laity do not gener-

ally believe that a valvular defect is always fatal (p. 158); it is misleading to call angina pectoris an affection of the arteries, so "that we may have anginal pains in any part of the body (p. 171). Between forty-five and sixty years of age is rather high for the average incidence of the disease. It is rather sweeping to say that "when a child is attacked by rheumatism the heart is almost invariably involved," p. 184). Such small points, however, hardly detract from the excellent presentation in a popular way of a difficult subject.

E. B. K.

THE ELEMENTS OF BACTERIOLOGICAL TECHNIC. A LABORATORY GUIDE FOR MEDICAL, DENTAL, AND TECHNICAL STUDENTS. By J. W. H. EYRE, M.D., M.S., F.R.S., (Edin.) Director of the Bacteriological Department of Guy's Hospital, London, and Lecturer on Bacteriology in the Medical and Dental Schools. Second edition: pp. 518; 219 illustrations. Philadelphia: W. B. Saunders Company, 1913.

THIS new edition of Dr. Eyre's well known and exceedingly valuable book on technique was occasioned by the growth of literature in recent years. The plan of the work is essentially the same as in the first edition. It can be used as a desk book by the student or individual worker, or as a guide for a teacher in laying out a course in practical bacteriology. The first part of the book is devoted to describing the behavior of the laboratory worker and familiarizing him with the surroundings and apparatus. Then follows a short description of the biological status of microorganisms, which is succeeded by an account of the manufacture of the media upon which they are grown. In natural sequence then are given methods of isolation, cultivation, identification, and inoculation of microorganisms. The eighteenth chapter is devoted to the study of experimental infection during life with which is included serology applicable also to natural human infections. The blood picture and temperature of experimental animals are given. Post mortem material is discussed next. A chapter is devoted to the special consideration of pathogenic bacteria. The final chapter and the appendix are among the most important and useful sections of the book. The former contains methods for the examinations of water, soil, foods, sewage, air, and disinfectants, including detailed lists of the necessary paraphernalia; while the appendix gives tables for weights and measures, computing thermometric scales, preparing dilutions, estimating pressure, and the use of antiformin. The book is well arranged, and the cuts are all clear and instructive.

H. F.

A MANUAL OF SURGERY. For Students and Physicians. By FRANCIS T. STEWART M.D., Prof. of Clinical Surgery, Jefferson Medical College; Surgeon to the Germantown Hospital; Out-Patient Surgeon to the Pennsylvania Hospital. Third edition; pp. 742; 571 illustrations. Philadelphia: P. Blakiston's Son & Co., 1913.

PREVIOUS editions of this book have received notice in these columns. It is intended for the undergraduate and the medical practitioner "seeking a guide to present-day surgery" and is admirably adapted to the purpose. The fact that a third edition is called for so soon after the second is good evidence of its excellence.

In the present edition, important additions have been made to many sections as demanded by the growth of surgical knowledge and experience. Under anesthesia, Crile's work on anoci-association receives mention. In syphilis, the reader is kept abreast of the most recent advances in diagnosis and treatment. So also in the chapters on surgical technic, the vascular system, the lymphatics, diaphragmatic hernia, fractures, the brain, the spinal cord, and amputations—as noted in the preface.

The author's large clinical and teaching experience have given him exceptional facilities for producing a book of this kind and keeping it a leader in its class.

E. B. H.

PRACTICAL BACTERIOLOGY, MICROBIOLOGY, AND SERUM THERAPY (MEDICAL AND VETERINARY). A TEXT-BOOK FOR LABORATORY USE. By DR. A. BESSON, formerly Director of the Bacteriological Laboratories of the Military Hospitals of France. Translated and adapted from the fifth French edition by H. J. HUTCHENS, D.S.O.; M.A.; M.R.C.S.; L.R.C.P.; D.P.H. (Ox.). Heath Professor of Comparative Pathology and Bacteriology of the University of Durham, Engld. Pp. 892; 416 illustrations. London: Longmans, Green & Co., 1913.

THE appearance of the revised edition of Dr. Besson's book in English will be welcomed by all bacteriologists who are familiar with the previous editions in French. The work is intended as a guide for the student and the more experienced worker in the detection and identification of pathogenic microorganisms. The translator has not only translated the French text but has added such material as he considered necessary or that has appeared since the French edition was issued. Dr. Hutchens' has been free in his translation and has achieved a most pleasing and fluent style, rather rare in scientific books. In former editions all theoretical matter was omitted but this issue contains a short chapter

upon the subject of immunity and the properties of immune serums, dealt with in an applied manner. The first quarter of the text is devoted to a full consideration of laboratory technique, of which the chapters upon the microscope and animal inoculation are especially good. The second part is devoted to the bacteria proper which are presented in groups according to their most pronounced characters, as for example the nonspore-bearing, Gram-negative, non liquefying rods, or the Gram-positive or Gram-negative cocci. The various organisms are described under the headings experimental inoculation, morphology, biological characters and detection. It would seem that too little space is given to the cultural characters in a book intended to be a laboratory guide. Much attention is given to the serum tests and the uses of antisera. An apparent slip is noted in the discussion of the *Pneumococcus*, where it is stated that this coccus does not ferment inulin, thus differing from the streptococci. The reverse is what is usually accepted. The next section is given to the higher bacteria and the description is fuller than is commonly found. The author uses the generic name *Discomyces* for the *Streptothrix*, an adoption not yet widely made in this country. The spirochætæ are discussed in the next section with the full details of their cultivation. The fifth division of the book covers the protozoa, emphasizing the comparative pathology and describing the metamorphoses of the individuals. The filterable viruses and the examination of water, sewage, and air are given in the sixth and seventh sections.

The book is a most excellent one and is the more welcome since nothing of the kind exists in English. The authors have presented all the acceptable techniques in a very practical manner. The recommending of certain ones, a characteristic of Besson's work, is admirable. It is to be regretted that the price is so high, for this may prevent the book from getting into the hands of students who would greatly profit by it.

H. F.

DORLAND'S AMERICAN ILLUSTRATED MEDICAL DICTIONARY.
 Edited by W. A. NEWMAN DORLAND, A.M., M.D. Seventh
 edition. Pp. 1107. Illustrated. Philadelphia and London: W. B.
 Saunders Company, 1913.

THE seventh volume of this up-to-date medical dictionary is not only up to the standard of its predecessors, but surpasses it. It contains several thousand more terms than the previous edition, and in addition there will be found a number of tables of tests, stains, and staining methods, methods of treatment, etc., all of

which should prove of value. A considerable amount of collateral descriptive matter has been included under the different headings, for example, under each drug are given its composition, sources, dose, etc., and a description of the structure of the different organs is given along with their function. The illustrations are excellent, and numerous, and the book as a whole deserves great commendation.

S. S.

HANDBOOK OF PHYSIOLOGY. BY W. D. HALLIBURTON, M.D., LL.D., F.R.C.P., F.R.S., Professor of Physiology, Kings College, London. Eleventh edition (being twenty-fourth edition of Kirkes' *Physiology*). Philadelphia: P. Blakiston's Son & Co.

THIS text-book is familiar to every teacher of physiology and thousands of students have obtained their fundamentals of physiology therefrom. Although thoroughly revised the bulk of the volume has not been increased, there being less than nine hundred pages of text. There is still a large demand for a book of this size, but the tendency recently has been to use text-books that contain much more subject matter, at least in the larger medical schools. Certainly more and more importance is assigned to the subject each year, and in this respect the book at hand does not follow the tendencies of the times. Nevertheless, the book has value, indeed great value, particularly to the student who wishes to review the subject on the eve of an examination, and to the busy practitioner who desires to look up, in the shortest possible time, a physiological point long since forgotten; for the book is splendidly arranged and carefully indexed. If he is satisfied with a rather superficial knowledge of the newer things being done in this subject, the volume is equally valuable and accurate.

In this edition the structure work is but little altered, nor is this necessary, for no book is more logical, or the descriptive material more lucid. Inevitably, however, new material must be introduced in a new edition of any work upon this subject, no matter how short the interval after the preceding one. And so here, the writer, has found this necessary, and revision has been undertaken not only in the right direction but also conservatively. Great changes are seen in the respiratory system, some in the chapter on circulation, and the chapter on reproduction is a new one. Nor have the chapters on digestion, kidneys, and special senses been neglected. Yet all this has been accomplished without increasing the size of the book, we see here how wonderfully conservative the writer has been.

E. L.

SURGICAL EXPERIENCE IN SOUTH AFRICA, 1899-1900. BY G. H. MAKINS, C.B., F.R., C.S.: Senior Surgeon to St. Thomas's Hospital, London; Vice-President of the Royal College of Surgeons of England, etc. Second edition; pp. 504, 28 plates; 105 illustrations: Oxford University Press: 1913.

THIS, the second edition, is practically a reprint of the first, except for the continuation of a few of the histories, and was gotten out because of the continued demand for the work.

The work is merely a recounting of a wonderful series of cases, chiefly of the bullet wound variety, in the personal experience of the author.

In the introduction is given an excellent description of the various bullets and rifles, their peculiarities of trajectory, penetration, vulneration and fatality in reference to their relative size and composition.

The author discusses in minute detail the affect of bullets, immediate and remote, in all parts of the body, the incidence of the great number of aseptic wounds, and their ultimate behavior if infection does occur. The advantage of the small caliber high velocity projectile to the person hit is conclusively shown by comparison with wounds from the older style rifle balls.

Wounds of the soft parts, bones, joints, nerves, vessels, head, spine, and abdomen are all given ample space for consideration and description. The chapters given up to vessel injuries are exceedingly interesting, especially the data concerning aneurysms and arteriovenous communications. The text dealing with bone injuries is richly supplied with a large number of very excellent reproductions of x-ray photographs.

The book is not intended for a text-book in any sense of the word, but merely a relation of a series of interesting and instructive facts gleaned from a very unusual personal experience of the writer. It is most instructive and affords interest to the reader throughout.

E. L. E.

SKIN DISEASES IN GENERAL PRACTICE. BY HALDIN DAVIS, Physician in charge of the Skin Department, Paddington Green Children's Hospital; Chief Assistant in the Skin Department, St. Bartholomew's Hospital; Assistant Physician to the Hospital for Diseases of the Skin, Blackfriars. Pp. 340; 62 illustrations. London: Henry Frowde; Hodder & Stoughton, 1913.

THE writer has classified diseases of the skin, in so far as possible, upon a typographical basis. He has arranged the subject in the following divisions: Introduction, including a cursory review

of the pathology; disease due to the common pyogenic organisms; eczema; syphilis; diseases giving rise to wide spread eruptions; eruptions affecting the face; eruptions affecting the limbs; diseases affecting the hands and feet; diseases of the nails; diseases with lesions on the pudenda and in the groins; diseases limited in extent but irregular in distribution; bullous eruptions; anomalies of pigmentation; diseases of the scalp: modern methods of treatment. Only the common diseases of the skin are included in the work. There is naturally a considerable amount of repetition, as some of the general diseases are also mentioned under the restricted regional divisions. The book contains seven excellent color photographs. A few of the black and white pictures are rather poor.

F. C. K.

AIDS TO GYNECOLOGY. By S. JERVOIS AARONS, M.D. (Edin.), M.R.C.P. (Lond.), Gynecologist to St. Anthony's Hospital, etc. Fifth edition; pp. 124; 4 illustrations. New York: William Wood & Company, 1913.

THE present volume which has reached its fifth edition contains much of service to the general practitioner. The arrangement of the chapters according to pathological rather than anatomical classification is to be commended. The symptoms, diagnosis, and treatment are dealt with as fully as possible, considering the limited size of the book.

S. J. R.

THE TONSILS AND THE VOICE. By RICHARD B. FAULKNER, M.D. Pp. 381. Pittsburg, Pa.: The Presbyterian Book Store, 1913.

It is an unpleasant task to be able to say nothing good about a book, but from the first page of this work, where the author's portrait appears as a frontispiece, it is a conglomeration of italics, quotations, and questions in large type with the answers, if there are any, so confused and jumbled up that it makes very tedious reading.

It is attempted to show, apparently, that the function of the tonsil is to aid in voice and tone production and that its complete removal is practically always followed by disastrous results. The book shows evidence of hard work, but as it stands it is thoroughly unscientific and worthy of scant consideration.

G. M. C.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Cultivation of the Organism of Epidemic Poliomyelitis.—S. FLEXNER and H. NOGUCHI (*Berlin. klin. Woch.*, 1913, 1, 1693) give the details of their successful attempts to cultivate the microorganism of epidemic poliomyelitis. (Only some of the more important facts can be given here.) The method which finally succeeded is one developed by Noguchi in the cultivation of spirochetes. Human aseptic fluid containing a piece of fresh sterile rabbit's kidney was the medium which proved most satisfactory. The exclusion of oxygen is necessary. For this purpose a deep layer of sterile paraffin oil is sufficient. The primary culture seemed to take with greater certainty where an aerobic apparatus was employed. The tubes were kept at body temperature. Flexner and Noguchi found that all tubes that showed turbidity, precipitation, or gas formation within one or two days were contaminated. Even tubes which remain clear or show slight turbidity may be contaminated. To exclude contaminations they removed small quantities of material with sterile pipettes and stained in the usual method, and also made transfers to the ordinary media. Bacteria in the smears or any aerobic growth are contaminations. Having excluded these, Flexner and Noguchi found that the growth of the poliomyelitis organism presented the following characteristics. After about five days in the incubator a faint opalescence is observed in the fluid about the piece of tissue. The controls remained clear or showed a finely granular precipitate about the tissue. In the following three to five days the opalescence in the inoculated tubes spread upward through the fluid while the precipitate in the controls collected more at the bottom of the tube. After ten to twelve days, the diffuse opalescence of the inoculated tubes began to clear

and a sediment composed of small particles of irregular shape collected at the bottom of the tube. By the use of about 0.2 c.c. of the primary culture, successful transplants can be secured. The material for inoculation was obtained from patients suffering with the disease and from experimentally infected monkeys. Some of the latter material was preserved nine months in glycerin. An emulsion made from this material after passage through a Berkefeld filter gave a positive culture. All the pure cultures obtained from the various sources were examined and showed similar characteristics morphologically and with dyes. In the dark field preparation it is possible with practice to distinguish the organism. It is best stained by Giemsa's or Gram's stain. The organisms are round in pairs, in short chains, or irregular conglomerate masses. The individual organisms reach a size of about 0.2 micron in diameter. The limit of optical definition in a microscopic preparation is between 0.15 and 0.3 micron. It is quite possible that smaller organisms than those observed may exist. In solid media chains are missed. As the culture becomes old, degenerative changes may occur. The organism described above is found so constantly in the central nervous system of diseased men or monkeys that the presumptive evidence of its etiological relationship is strong. In attempting to reproduce poliomyelitis in monkeys cultures which were obtained from human sources as well as from monkeys were used. Inoculations were made directly into the brain or into the nervus ischiadicus and peritoneal cavity. As was to be expected the material obtained from man proved less infectious than that which had already been passed through monkeys. Positive results were obtained with each method of inoculation equally frequent. Cultures which were in their eighteenth or twentieth generation caused the disease to appear in monkeys. Tissues from these infected monkeys were proved to be infective. Furthermore, all the characteristic histological changes of the experimental infection were reproduced in the infected monkeys.

The Production of Acetone Bodies in the Living Animal.—F. FICHLER and H. KOSOW (*Deut. Arch. f. klin. Med.*, 1913, cxi, 479) conclude from their experimental studies in part as follows: The liver is the organ where acetone and diacetic are formed in the body. It has already been shown that the perfused liver is capable of forming these substances. Furthermore, it is in the liver that B-oxybutyric acid is formed. It is probable that this acid is produced chiefly in the liver, though it is not certain that other organs or tissues are not also concerned in its formation. The fact that an animal whose liver function is partially destroyed produces less of these bodies than one in whom the liver function is normal supports the view expressed above. In so-called reversed Eck's fistula the liver produces excessive amounts of acetone bodies.

The Fatiguability of the Kidneys.—H. MOSENTAL and C. SCHLAYER (*Deut. Arch. f. klin. Med.*, 1913, cxi, 217) have made an experimental study of the fatiguability of the kidney with the following results: The diseased kidney may be exhausted in various ways. The state of renal function determines very largely which diuretic fatigues the kidney and which does not. The kind and frequency of use of the

irritant employed to produce the kidney lesion is also an important factor, as well as the dose of the diuretic. An excess of sodium chloride may increase the fatiguability of a diseased kidney (chromium poisoning), even though it is well excreted. This fatiguability of the kidney is shown experimentally only after giving caffeine. In other cases caffeine may restore to activity a kidney fatigued by sodium chloride.

The Secretion of Urotropin by the Mucous Membranes.—A. LEIBECKE (*Berlin. klin. Woch.*, 1913, 1, 1698) has attempted to determine whether urotropin is secreted in concentration sufficient to inhibit bacterial growth, especially in the middle ear. His results are summarized as follows: (1) Urotropin appears in the urine about one-half hour after it is administered, in the cerebrospinal fluid after three-quarters of an hour, in the milk in one hour, in the ear and bronchial secretions after about two hours and in peritoneal exudates after about four hours. It disappears from the secretion of the ear after fifteen hours, from bronchial pus after thirty hours, from the milk after twenty-one hours, from cerebrospinal fluid after fifty-three to seventy-seven hours. The time intervals are only approximate. (2) The greatest concentration is contained in the cerebrospinal fluid and milk soon after giving the drug. In the exudate from the middle ear, this point is reached only after four to six hours. The same apparently holds true for bronchial pus. (3) In doses of 0.25 to 1 gram the maximum concentrations observed were 1 to 10,000 in the ear, peritoneal pus 1 to 12,000, 1 to 15,000 in cerebrospinal fluid, and 1 to 20,000 in bronchial exudate; the concentration in the milk is the lowest. (4) The concentration of urotropin in cerebrospinal fluid and aural pus in the child in doses of 0.25 and 1.5 grams bears no quantitative relation to the dosage. The body weight of the patient also appears to be of no consequence. (5) No cumulative effect is demonstrable in milk, cerebrospinal fluid or aural pus. (6) It is recommended to give relatively large doses within six or seven hours. (7) In concentration on 1 to 10,000 to 1 to 6000 in aural pus the effect on bacterial growth is doubtful. (8) Injurious effects on kidneys are conceivable with the usual therapeutic dose, but the danger of this is very slight if the patient drinks freely of water.

A Contribution to the Radiological Examination of the Pericardium.—E. v. CZYHLARZ (*Wien. klin. Woch.*, 1913, xxvi, 1394) finds that during deepest inspiration a clear space is seen between the shadow of the diaphragm and that of the heart extending from the apex to the vertebral column in about 75 per cent. of normal individuals. The phenomenon is apparent only for one to two seconds and is lost soon as expiration begins. It is difficult to photograph it satisfactorily, but with practice it can be detected readily with fluoroscopic examination. The phenomenon is due to separation of the two layers of the diaphragm, one of which is attached to the diaphragm, the other to the heart. The presence of the phenomenon, therefore, excludes the possibility of an adhesive pericarditis involving this area. As the phenomenon may not be observed in a certain proportion of normal individuals, its absence is without significance.

The Transmission of Experimental Syphilis to Man.—A. BUSCHKE (*Deut. Med. Woch.*, 1913, xxxix, 1783) considers that Metchnikoff's experiments which tend to show that experimental syphilis is not transmissible to man are inconclusive. He reports a case which came under his own observation which seems to prove the contrary, and believes that it would be very unwise to employ spirochetes from experimental syphilis for vaccination of man, as Metchnikoff has suggested. Buschke was consulted by a man who was employed as assistant in a laboratory in which experimental syphilis was being studied. The patient was thirty years of age, married, and has previously enjoyed good health. He denied venereal infection. April 7, 1913, the patient was assisting at an operation on a syphilitic rabbit. The operator inserted a sterile needle into the syphilitic testicle. As the needle was withdrawn, it was accidentally plunged into the skin of the end phalanx of the patient's left index finger. The patient wore rubber gloves which were immediately removed; blood was squeezed from the small wound, which was then washed with bichloride of mercury and with carbolic acid. Finally the finger was bandaged. The wound healed and nothing more was thought of the accident. About the middle of June the patient began to feel badly. He complained of night sweats, pains in the head, especially above the eyes, and vague general distress, which suggested to the patient influenza. At this time the patient had noticed a small nodule about the size of a pin-head beneath the skin of the last phalanx of the left index finger. By the end of July the general malaise had increased to such a degree that the patient spent his week's vacation in bed. The patient himself now suspected syphilitic infection but did not express his fear and was referred to an oculist because of the constant pain above the eyes. There was now a bluish discoloration about the ulcer on the finger. When Buschke was first consulted August 4, 1913, he found on the left index finger a livid, oval area about 0.5 by 2 to 3 cm. in extent, sharply circumscribed. The skin was slightly elevated, and there was induration. In the left inner cubital region there was a firm, indolent gland about the size of a walnut. Over the abdomen were several erythematous spots. The Wassermann reaction gave complete fixation. In the next few days a maculopapular eruption appeared on the buttocks and extremities. The genital organs and inguinal glands were normal. In the serum obtained from a papule spirochetes were found. The syphilitic infection from which the patient is suffering is quite as virulent as usual, and there can be little doubt that it was contracted in the manner described. The case demonstrates that the disease produced in rabbits by inoculation with human spirochetæ pallidæ is certainly syphilis; that repeated passage through animals does not lessen the virulence of the organisms for man; and that a living vaccine obtained from animals cannot be employed in man.

Hypersensitiveness to Arsenic.—C. STAUBLI (*Deut. med. Woch.*, 1912, xxxviii, 2452) reports two patients treated with sodium cacodylate, in whom acute symptoms developed following injection of the drug. Their hypersusceptibility to the drug resulted in extensive local inflammatory swelling, marked rise in temperature, general malaise, headache, diffuse pains in the joints, loss of appetite, and, in one case, dyspnea.

S U R G E R Y

UNDER THE CHARGE OF

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The Transplantation of the Hair-covered Skin.—PERIMOFF (*Zentralbl. f. Chir.*, 1913, xl, 1443) says that Lauenstein attempted, unsuccessfully, to transplant hair-covered skin from one man to another. He then tried experiments on nine dogs, with indifferent success. On April 6, 1912, Perimoff removed an ugly, star-shaped scar, completely hairless, 10 cm. long and 5 cm. wide, from the temperoparietal region of the scalp, going down to the bone. The patient had requested the operation and had brought with him a man, who, for a consideration, was prepared to sacrifice a portion of his scalp for transplantation to the patient. Healing occurred by first intention and in ten days the patient left the hospital. He returned ten days later when the flap was grown fast. The hair had not fallen out and its growth left nothing to be desired. The patient, an officer, gave his word that he would report again if the hair fell out, but up to the time of the report he had not appeared. Perimoff believes that Lauenstein's failure was due to the fact that the latter used iodobenzine in the disinfection of the skin and that the skin was too much traumatized. Similar experiments on dogs may fail easily because it is difficult to maintain in dogs the unchanged position of the transplanted skin.

The Commandments of Modern Urinary Practice.—CATHELIN, of the Hôpital d. Urologie, Paris (*Amer. Jour. Urology*, 1913, ix, 437) has collected the following principles or commandments, which he offers, particularly, to the general practitioner: (1) Never pass a catheter the first time you see a patient unless compelled. Close clinical examination will almost always enable us to arrive at a diagnosis without it, while its use may lead to very troublesome infection. (2) Never catheterize during an acute attack of gonorrhea. As a rule this procedure is the means of conveying infection to the deeper parts giving rise to prostatitis and spreading to the neck of the bladder and ultimately to the bladder itself. It is in these cases that we must make generous use of purely medical means (diuretics, the balsams and antiseptics). (3) Never syringe the anterior urethra during the acute stages of gonorrhea, for the pus may thus be washed back into the deep urethra which then soon becomes infected in turn. (4) Never dilate when there is too much resistance. A narrowed canal which

yields to gradual dilatation, gives quite contrary results if forced. (5) Never cocaineize the canal without urgent reasons. Cathelin has never introduced cocaine into the urethral canal. A patient who has pain when catheterized is the victim of bad catheterization. (6) Never omit rectal examination in urinary subjects. This method of examination puts us on the track of the diagnosis and enables us to steer clear of gross mistakes. (7) Always explore with a metal sound when the patient complains of pain in the glands. Spontaneous pain in the glands provoked by passing water is a pathognomonic sign pointing, almost to a certainty, to stone in the bladder. Of course this does not apply to young subjects with gonorrhea, where this pain is customary, for other reasons, but in middle-aged people we must suspect calculus. (8) Always resort to cystoscopy in doubtful cases. There are indeed cases in which no diagnosis is possible otherwise than by actual inspection, such as polypi, ulcers, etc. (9) Always resort to cystoscopy in hematuric patients at a suitable period. In vesical hematuria the suitable period is between the attacks of bleeding, in renal hematurics it is during the actual bleeding in the beginning, because at first the hemorrhages are less profuse and their discovery will enable us to decide which kidney is affected, though this kidney cannot be felt and gives no pain. (10) Always radiograph the upper urinary apparatus in renal cases of uncertain diagnosis. Cathelin regards cystoscopy and the metal sound as sufficient and even preferable for the lower part of the genito-urinary tract. (11) The tuberculous kidney is a small kidney, not palpable and not painful. It may only be manifested by more or less marked cystitis. (12) Evening hematuria is always a calculous hematuria, *i. e.*, hematuria which comes on of an evening is usually bleeding, provoked by the day's work, so that it may fairly be opposed to spontaneous hematuria due to tumor. (13) Never make use of silver salts in urinary tuberculosis. Nitrate of silver while remarkably affective in common affections of the urinary tract, is altogether contra-indicated in tuberculous affections. They get worse when it is used. (14) Tuberculous urine is never ammoniacal. It has no odor.

A Contribution to Malignant Tumors of the Testicle, Especially the Epitheliomatous.—SAKAGUCHI (*Deutsch. Zeits. f. Chir.*, 1913, cxxv. 294) says that the so-called large-celled tumors are the most frequent type of malignant tumors of the testicle (23 out of 32 tumors). The typical large-celled tumors are epithelial and specific for this organ. Because of their situation, the age of the patients, the manner of extension of the tumor cells, and their similarity to the cells of the convoluted tubules, these tumors, in all probability, develop from the epithelium of these canals. Complicated epithelial tumors are found in the testicle, which are made up partly of cuboidal partly of cylindrical tumor cells, and are probably developed from the epithelium of the tubuli recti or canals of the rete testis. This is shown by the site of the tumor, the frequent intracanalicular method of extension of the tumor cells of the rete portion, the cuboidal and cylindrical cells, and the colloidal contents of the same, as well as the similarity of the tumor growth to the exuberances in the regeneration of the rete canals. Sarcoma is found very rarely in the testicle. Only

one occurred in this group of 32 tumors of the testicle. The simultaneous occurrence of cancer and tuberculosis was found only in 1 case. No relationship between the two conditions could be established. It is probable that the tuberculosis was secondary. Glycogen was never absent in the recent large-celled tumors. Even when the preparations were kept a long time in unsuitable fixation fluid, glycogen could be found in a large number of cases. On the other hand, fat could be found only in tumor cells already undergoing degeneration. Elastic fibers in the tumor foci (in sarcoma as well as cancer) were always diminished and finally disappeared. Intracellular infiltration was found in only 5 cases, and then it was not marked. The large-celled epithelial tumors occurred most frequently in the age of greatest strength, the fourth and fifth decade. In 4 cases, the tumor was associated with a history of trauma, in 1 with ectopy. In 13 cases the tumor was on the left side. In 8 the history does not show the side affected.

The Treatment of Dislocation of the Humerus with Fracture of the Head.—CAHEN (*Deutsch. f. Chir.*, 1913, cxxv, 391) says that he has twice, in the past year, made the attempt, after separating completely the fractured head from its ligamentous and other attachments, by placing it in good position on the fractured surface of the lower fragment, to obtain good union. In the first case, a man, aged fifty-two years, this was successful notwithstanding the development of delirium. The functional result, a year after the injury, is so good that the patient has resumed his work in a machine shop. In the second case, a woman, aged sixty-three years, there developed six weeks after complete healing, a fistula in the operation scar. The head of the humerus did not remain fixed in its proper position, and a large fragment was removed a half year later. The active movements of the injured arm at the shoulder are now much limited. In the first case, the x-rays show that the upper end of the humerus is still in the dislocated position. The patient can raise the operated arm forward to 20 degrees above the horizontal. Passively, the arm can be raised completely.

Operation on Perforated Stomach and Duodenal Ulcers.—SEIDEL (*Zentralbl. f. Chir.*, 1913, xl, 1481) says that the two chief indications in the early operative treatment of these perforated ulcers, are: To close the perforation, and to reestablish the conditions which will prevent postoperative obstruction to the escape of the stomach contents into the intestine. The most reliable method of closing the perforation is always by suture. Seidel has never found it necessary to deviate from this principle, and succeeded in thus closing the perforation, without great difficulty, in 19 cases. It is not necessary that specially favorable conditions must be present. He found in some of his cases callous changes, very large ulcers, as well as saddle-shaped ulcers of the lesser curvature with perforation on the posterior wall. He says that the closure of the perforation depends alone on the technique. The sutures must be placed as far as possible from the edges of the perforation. In very small ulcers the sutures should encompass all the callous tissue. In very large ulcers it should grasp

the greatest part of this tissue and turn it in. The first row of sutures are made with thick silk and pass through the whole wall of the stomach into its lumen. A row of sutures reaching to the non-infiltrated tissues, or a flap from the greater or lesser omentum, reinforces the through-and-through sutures. In his last 7 cases he employed the following method of preventing cutting of the sutures: On two sides of the circumference of the perforation, 1 cm. or more from the edges of the perforation, are passed one or two supporting sutures, somewhat parallel to the margins of the perforation and reaching to the lumen of the stomach. They are not tied tightly enough to fold or cut through the friable tissue. The real closing sutures, also of silk, are then passed from one side to the other, *i. e.*, at right angles to the supporting sutures, reaching outside of the latter and passing through the stomach wall into its lumen. If these are not tied too tightly the perforation is closed without danger of the sutures cutting through. A row of Lembert sutures or an omental flap will complete the watertight closure of the perforation. In 14 of his 19 cases, in which he employed the sutures without further aid in closing the perforation, there have been up to the present time, no disturbances in the passage of the stomach contents, not even in cases in which there had been a marked stenosis at the pylorus.

Alcohol for the Prevention of Acute Cocaine Poisoning.—HERZFELD (*Zentralbl. f. Chir.*, 1913, xl, 1705) says that he has obtained repeatedly from minimal doses of cocaine (Seleich's infiltration narcosis), mild symptoms of poisoning. Dentists have had a large number of deaths from this cause. From inquiry of a number of surgeons he found that some regarded morphin as the antidote *par excellence*, and that an injection of morphin was completely sufficient in these cases. Herzfeld says that morphin has caused many deaths in many cases of cocaine and atropine poisoning. He gives every patient, without exception, 25 to 50 c.c. of whisky or cognac, by the mouth, before the first injection of cocaine. In long-continued operations he repeats the dose, mixing the whisky with sugar water in women and children. In the course of the last four years, he has not had the slightest trouble from local anesthesia with cocaine.

Interparietomuscular Pyloropexy as a Method of Closing the Pylorus in Gastroptosis with Gastrectasia.—MARIANA (*Zentralbl. f. Chir.*, 1913, xl, 1706) says that he operated on 2 cases with death from ether pneumonia in the first, and in the second healing with the best functional results. After performing a posterior gastro-enterostomy near the pylorus, he fixes the sharply bent pylorus by suturing it to the margins of the right rectus muscle in the wound, a little below the costal arch. The fixation of the sharply flexed pylorus in the abdominal wound, closed the pylorus, served as a suspension, and thus improved the function of the gastro-enterostomy. In his second case, it was shown by the x-rays that the greater curvature of the stomach, before the operation, reached almost to the pubis, while after the operation it extended to about the umbilicus and occupied a transverse position. The x-rays showed also that the bismuth food no longer passed through the pylorus but through the anastomotic opening.

THERAPEUTICS

UNDER THE CHARGE OF

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Clinical and Laboratory Salvarsan Relapses and their Remedy.—HEIDINGSFELD (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1598) is firmly of the opinion that no case of syphilis can be satisfactorily treated unless the treatment is controlled by the Wassermann reaction. In 651 cases, 3304 Wassermann examinations were made, and salvarsan was administered 952 times. The administrations were made in ambulatory private practice and not a single administration was attended by any incident of untoward character. The initial dose was almost uniformly 0.6 gm. of salvarsan and 0.9 or 0.6 gm. of neosalvarsan; if neosalvarsan was repeated within from thirty to sixty days, 0.3 gm. was usually administered, unless persistent lesions or an unchanged or strongly positive Wassermann indicated otherwise. A Wassermann examination was made prior to the initial administration and was repeated every thirty days, until the blood became negative. When the fixation test remained negative two successive times, the examination was repeated in sixty days, if then negative, in ninety days, and then at intervals of six, nine and twelve months, according to the special indications of the case. Deducting 209 cases which were observed less than ninety days, or could not be intelligently followed for the reason of only one Wassermann examination, in 339 out of a total of 442 cases, or 77 per cent., the patients proceeded to recovery from a combined clinical and laboratory point of view, as a result of one or more administrations of salvarsan. No other adjuvant was employed, although 276 cases of somewhat long standing received some form of antisyphilitic treatment prior to the administration of salvarsan. Of the 103 cases, or 23 per cent., of salvarsan failures, nine received no additional attention. Of the remaining 94 cases, 13 proceeded to clinical and laboratory recovery with the aid of mercurials and 23 with the aid of atoxyl and sodium cacodylate: 21 have been observed comparatively too short a time to pass definite judgment; 22 cases have apparently failed, from at least a laboratory point of view, with all methods of treatment. Summarized, in 50 per cent. of salvarsan failures the cases have proceeded to complete clinical and laboratory recovery when the treatment was supplemented by other measures. In 371 cases, for the most part old and long-standing infections, some form of previous mercurial treatment has been received. Of these, 230 cases proceeded to recovery and 95 could not be intelligently followed. In other words, 83.5 per cent. proceeded to absolute recovery from a clinical and laboratory point of view. This is of striking interest, as it shows that more cases (83 per cent.) proceeded to salvarsan recovery when previously treated with mercury, than those cases (61 per cent.) which had received no previous mercurial

treatment. This past apparently indicates that previous mercurial treatment favorably influences syphilis for salvarsan treatment. It may be, however, that the percentage of recovery is higher in the cases previously treated with mercury for other reasons: A large percentage of these cases were of rather long standing, with weak positive, negative or almost negative Wassermann. Some possessed a dubious history, enveloped in greater obscurity by a too early administered mercurial treatment. The cases not previously treated with mercurials were, almost without exception, comparatively recent infections, personally observed, in which present-day methods of greater accuracy substantiated the diagnosis. It is evident from this that salvarsan failed to effect a satisfactory result from a clinical and a complement-fixation point of view, in 23 per cent. of the cases treated, and salvarsan aided by other measures in about 12 per cent. Some of the "failures" were in cases which were rapidly advancing in spite of treatment. The majority of the "failures" however showed no clinical manifestations but gave a persistently strong positive Wassermann. Heidsieck believes that salvarsan, though not an unfailing remedy, is by far the most effective agent which we possess for the treatment of syphilis. It effects an apparent clinical and laboratory cure in about 77 per cent. of the cases treated. A large proportion of the remaining 23 per cent. of cases with the aid of other measures, gives every promise of proceeding to a negative Wassermann and absolute clinical cure in due course of time.

The Dose and Methods of Application of Radio-active Substances in Internal Medicine.—GUDZENT (*Berlin klin. Woch.*, 1913, 1, 1597) has experimented in order to secure a more uniform dosage of radium emanations as given by inhalation. He believes that doses of from three to five Maché units per liter are as efficient therapeutically as the higher concentrations. He also says that nervous and anemic patients do not seem to bear the larger doses as well, and since they are no more effective therapeutically, he advises against their use. He believes that the most efficient method of giving the radium is by inhalation. Gout and chronic articular rheumatism are most influenced by radium treatment and especially when the radium is given by inhalation. Sciatica, diabetic neuralgias, and Basedow's disease are also very much improved by this method of treatment. With reference to the use of other radio-active substances such as thorium and tharium X. Gudzent is of the opinion that the results obtained with their use have been decidedly inferior to those obtained with radium.

Therapeutic Pneumothorax as a Palliative Measure.—DUNHAM and ROCKHILL (*Jour. Amer. Med. Assoc.*, 1913, lxi, 826) report 20 cases of pulmonary tuberculosis treated by artificial pneumothorax. The article emphasizes the value of this treatment as a palliative measure and the value, almost the necessity, of safeguarding the treatment by the use of the Röntgen rays. In emphasizing therapeutic pneumothorax as a palliative measure they do not deny its value as a curative one, but they do not feel that they have had sufficient time, experience or results to attribute to it this superlative value. They

say that the results and effects of this therapy are positive. The principal pathological findings after collapsing the lung are that the cavities are emptied, in part or in whole, according to the extent of the pleural adhesions, caseous areas have become cicatrized, and above all, an extensive overgrowth of the fibrous tissue is permitted during the enforced rest of the lung. The clinical effects of the induced pneumothorax are shown by a fall in temperature and a reduced number of night sweats, increased strength and appetite and finally gain in weight. These effects are all due to lessened absorption of toxins. The cough and sputum are greatly lessened and the number of tubercle bacilli in the sputum diminish. This treatment is of especial value in the control of pulmonary hemorrhages. Cases for this method of treatment should be carefully selected, but the indications for the proper selection of suitable cases is, as yet, not entirely clear. They consider frequent Röntgen-ray examinations most important in order to determine the proper time for refilling. The amount of nitrogen injected should be just sufficient to keep the lung collapsed and no more. Dunham and Rockhill conclude that this treatment is palliative and offers relief when usual methods of treatment have been unsuccessful. While it will possibly never become a routine treatment for tuberculosis, its use will certainly be indicated for those with quiescent lesions of one side and acute recrudescence of the other, and for such advanced cases as may at least profit by the certain amelioration of clinical symptoms. By the use of stereoscopic röntgenograms it is possible to select cases suitable for the treatment, to watch the progress of the disease, to determine the extent of the lung collapse, to note the pressure on the heart and mediastinum, to exclude pleural effusion and especially to watch the progress of the disease in the uncollapsed side.

The Röntgen Ray Treatment of Ring-worm.—EMRYS-JONES (*Brit. Med. Jour.*, 1913, pp. 849, 2753) basing his conclusions upon 200 cases of ring-worm treated by Röntgen rays, considers that this is the best and much the greatest method of treating this disease, particularly when the disease is extensive and well-established. He uses the single dose method, that is one exposure is given to any portion of the infected area. At times a single exposure is incomplete and this necessitates further treatment. He has never had a burn, although 93 of the cases were infected over the entire scalp. The technic and details of this method are given in the article. Emrys-Jones says that, with proper apparatus and in expert hands, this method is perfectly safe.

Pneumothorax Treatment of Tuberculosis of Lungs.—AMREIN and LICHTENHAHN (*Quart. Jour. Med.*, 1913, vi, 487) report 11 cases of pulmonary tuberculosis in which they produced an artificial pneumothorax by injecting nitrogen for purpose of treatment. The cases are reported in detail. In six of the eleven distinct and marked benefit was obtained. The chief results of the treatment were the disappearance of fever and other toxic symptoms, the diminution of cough and expectoration and the checking of hemoptysis when it was present. The remaining five cases were not so definitely successful. Amrein and Lichtenhahn believe that by this method of treatment many

apparently hopeless cases of pulmonary tuberculosis can be arrested, and, further, may be healed and even if satisfactory results are few and far between, the trial of the treatment is legitimate. The article also includes a short résumé of the literature upon the subject of induced pneumothorax and Amrein and Lichtenhahn discuss briefly the different methods of producing it. They prefer the Murphy-Brauer method by a preliminary incision down to the parietal pleura. The induction of an artificial pneumothorax must always be controlled by a suitable manometer. The amount of gas introduced into an individual case is dependant upon the presence or absence of pleural adhesions and they have injected as much as 1000 c.c. of nitrogen. It is also important to have an x-ray examination before an attempt is made to produce a pneumothorax principally to determine whether the other lung is sound or not. Moreover the x-rays are of great value in comparing conditions at subsequent refillings of the pleural cavity.

Eucalyptus Oil in Scarlet Fever and Measles.—ELGART (*Med. Klin.*, 1913, ix, 1251) acting upon Milne's suggestion has used eucalyptus oil for the prevention of scarlet fever and measles. Milne advised inunction of the entire body with the oil but Elgart has had equally good results by the use of a bag soaked with the oil which is worn around the neck by those exposed to contagion. In this way the children inhale the fumes constantly and the room is kept saturated with the fumes. Milne during the past thirty years has had 245 cases of scarlet fever and 234 cases of measles in a total of over 12,000 admissions to boys' homes of which he is in charge. The cases were all imported and no epidemic resulted even without isolation of the sick children. This result was attained, according to Milne, by merely rubbing the patients from head to foot with the eucalyptus oil twice a day for the first four days and then once a day for six days. In addition the tonsils were swabbed with 10 per cent. phenol in oil, at first every two hours and then at longer intervals. Elgart advises the use of the eucalyptus oil for everyone exposed to the infection in addition to its use by the patients themselves. He also prefers the inhalation of a 30 to 50 per cent. solution of lime as a means to free the throat from the infecting bacteria and advises these inhalations as a prophylactic measure. In brief Elgart would not only render the patients themselves less contagious but would render those exposed to contagion less apt to contract the disease. With respect to the treatment of scarlet fever—Elgart says that few of his scarlet fever patients, on systematic inhalations of lime, developed complications and those complications which developed were mild and short in duration. He believes that his method is efficacious in preventing the spread of infection, in shortening and attenuating the course of both scarlet fever and measles. Milne's method is, according to Elgart, especially adapted for the prevention of scarlet fever and measles in various institutions.

"Specific" Use of Salicylates in Acute Rheumatism.—MILLER (*Quart. Jour. Med.*, 913, vi, 519) in an endeavor to answer certain objections that have arisen with regard to the action of the salicylates in acute rheumatism, says that the objection that the larger doses

of salicylate do not imply increased absorption of the drug is without foundation. The objection that the larger doses are too prone to produce vomiting to be of value is only partially true. The production of vomiting is more a matter of the type of case under treatment and the methods of administration than the size of the dose employed. The vomiting produced in severe cardiac cases must necessarily be a limitation to any anti-rheumatic action which the drug may possess in rheumatic carditis. The objection that large doses are too prone to produce acid intoxication to be of value is also only partially true. The method of administration is of more importance than the size of the dose. The objection that the larger doses are dangerous and tend to increase fatalities, is not supported by the series of cases Miller examined. It is again a question of knowing how and when to use the drug. The objection that the specific use of salicylate is unsound, as relapses, particularly of nodules, are not prevented, is not well supported by the series of cases examined. Most of the relapses occurred on or after small doses or a short period of administration of the drug; cases taking large doses showing some immunity to relapses. Nodules are not generally more commonly found in relapses than are other manifestations, and where they develop under large doses it seems that they signify little, if any, fresh activity on the part of the infection.

PEDIATRICS

UNDER THE CHARGE OF

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The Meningeal Form of Poliomyelitis.—ARNOLD NETTER (*Brit. Jour. Child. Dis.*, 1913, x, 531) discusses the meningeal forms found in the epidemic of poliomyelitis existing in France for the last four years. Wickman defined the "meningeal form" as those cases simulating cerebrospinal meningitis, simple meningitis, or even tuberculous meningitis, with the symptoms of violent onset, high temperature, vomiting, headache, pains in the back and limbs, rigidity of trunk and neck, and Kernig's sign. Paralysis usually appeared after several days and might be transitory and ill-marked, but was more frequently persistent and followed by muscular atrophy and deformity. In some cases the clinical picture remained that of meningitis exclusively, whether recovery or death took place. The pathological anatomy of cases fatal at an early stage has always shown the pia mater infiltrated with cells, and lumbar puncture shortly after the onset shows an albuminous and fibrinous fluid rich in cellular elements. An erroneous diagnosis of cerebrospinal meningitis has been made in a number of cases. The cerebrospinal fluid gives valuable information. In a fair number of cases of meningococcal meningitis the fluid is almost trans-

parent during the first thirty-six hours, and contains only a few cells. On the other hand, the fluid in the early stages of these cases of poliomyelitis is definitely fibrinous and rich in cells, many of which may be polymorphonuclears. Great importance is attached to the knee jerks which are often lost at an early stage, and to the presence of pain in the limbs which appears more marked than in other forms of poliomyelitis. The seasonal incidence is of value, poliomyelitis being more frequent in summer and autumn and meningitis in the spring. The co-existence of typical cases is also a help. Poliomyelitis with meningeal onset has been especially frequent in France. In one study of 58 cases it was found in 29 per cent. In other studies throughout France the percentage has been at least as high. Several epidemics erroneously termed cerebrospinal meningitis have subsequently shown their true character by the development of muscular paralysis and atrophy.

Whooping Cough in the First Days of Life.—E. A. COCKAYNE (*Brit. Jour. Child. Dis.*, 1913, x, 534) furnishes interesting testimony of older writers on congenital whooping cough. He cites a number of writers, such as Sir Thomas Watson, Rillet, and Barthé, who mention infants who had characteristic fits of coughing on the first day of their lives, the mother having had whooping cough during the last months of pregnancy. The case described by Cooper Cole was probably congenital. The mother developed pertussis in the sixth month of pregnancy. The child, born at the eighth month, began to cough on the third day, and whooped on the seventeenth day, the attack being typical and severe. If this case were congenital it would show that the organism may be found in the circulating blood or remain virulent in the placental tissues for nearly two months after onset of disease. Pertussis in the newly born acquired after birth is more numerous, but even this is seldom met with. Bouchut reports a case in which an infant aged four days, two days after exposure to infection, began to cough and whooped eight days after birth. Numerous cases are mentioned where infants developed pertussis when ten, twelve, and fifteen days old. Cockayne reports a case of his own in which the infant began to cough at the age of five days. The incubation period must have been four days or less, its mother and a brother developing the disease a few days before its birth. The disease in the infant was typical and the blood examination showed a characteristic leukocytosis with increase of the lymphocytes. The disease in young babies is often atypical, there being no "whoop," but a more paroxysmal character in the coughing than is usual in mere bronchitis.

"Tic" in Children.—PHILIP F. BARBOUR (*Pediatrics*, 1913, xxv, 697) illustrates several cases of "tic" and shows the difference between this condition and chorea. In the case of a girl said to have chorea, the prominent symptom was a quick movement of the head from side to side every few minutes. The fact that the child had rheumatism might further complicate the diagnosis. The following tests, however, indicate the differentiation. When her tongue is protruded it is held perfectly still and she has perfect control of its

movements. In chorea it would be protruded in an uncertain and irregular manner, and would probably be drawn into the mouth quickly without apparent control. In her hand-grip there is no irregularity or failure in coördination in reaching for the hand, as would be the case in chorea, and the contraction is firm and persistent. When asked to do voluntarily the movements of the head which she appears to be doing involuntarily, she moves her head from side to side with perfect rhythm and regularity. There is no exaggerated jerking of the head as in chorea. In another case referred to the face was grimaced. Barbour mentions here the relationship between local irritation and this form of tic. Cures have frequently followed operations which relieved the irritation and whether it is true or not that the basic factor is a neuropathic substratum, one should persist in removing local causes of disturbance. In chorea there is inability to coördinate the muscles for a specific purpose. In tic there is coördination to procure certain results, but coördination is repeated until it becomes impulsive rather than volitional. The inability to resist the desire to make certain coördinated movements assumes a type of obsession, a basic factor differing markedly from chorea, and placing the disorder within the realm of psychical defects. The original purpose for establishing a habit of coördinating certain muscles is hard to determine, but may be the itching of an eyelid, or the wearing of a tight collar which induces a shrugging movement. Patrick, of Chicago, suggests the most rational treatment in these cases. It consists in making the movements volitional, so that instead of remaining as an unconscious habit, the patient will think about the movement he makes. No treatment offers very optimistic results in these cases, but the method mentioned seems to offer the most favorable outcome.

Pyuria in Infancy.—THEODORE J. ETTERICH (*Pediatrics*, 1913, xxv, 702) makes a plea for the more careful and routine examination of the urine in young children because of the frequency of acute pyelitis and the fact that many of these cases are mistaken for typhoid fever, malaria, and dentition fever. His remarks are based on 19 cases of acute pyelitis under his observation. All were females and ranged in age from seven months to eight years. The condition may be primary, but is often secondary to gastro-intestinal disorders, influenza, and other infectious diseases. The colon bacillus was found in 4 of his cases. In very young children this condition is remarkable for its lack of distinctive features. Fever is usually high and of the remittent type, and continues in the acute cases from three to six weeks. No chills, convulsions, or nervous symptoms occurred in any case, and there was nothing to explain the fever until the urine was examined and pus was found. The urine is very acid in reaction, the specific gravity usually low, and numerous pus cells and albuminous debris is found. The general health was, as a rule, not markedly impaired. Pus was often present in the urine several weeks after the patient had fully recovered. There were no relapses and no deaths. The treatment was potassium citrate gr. v every three hours until the fever subsided. Then urotropin in 1-grain doses four times a day.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Puerperal Sepsis at the Sloane Hospital for Women.—WILBUR WARD (*Amer. Jour. Obstet.*, March, 1913) states that in the last 8000 cases at the Sloane Hospital the septic mortality was 0.0485 per cent. A marked decrease in mortality and morbidity followed the routine use of rubber gloves. Another striking point is the fact that in cases treated by Cesarean section previous examination and manipulation greatly increased mortality and morbidity. Section should be declined in cases that have been much interfered with before they are brought to hospital. In prophylaxis, surgical asepsis is strictly used, and all interference, whether by examination or douching or the use of instruments, is limited as far as possible. In the presence of sepsis uterine drainage should first be secured by vaginal or intra-uterine douches with salt solution. If no improvement follows the uterus should at once be explored, and only once with the gloved finger, and then in the gentlest manner possible. Should secondary foci arise they are to be treated in accordance with the circumstances of each case. Especial stress is laid upon the general supporting treatment.

Rupture of the Uterus.—An interesting case of rupture of the uterus in early pregnancy is reported by NOON, in St. Bartholomew's Hospital (*Jour. Obstet. and Gynec. of the British Empire*, October, 1912). The patient was supposed to be pregnant about three months. Hemorrhage was followed by pain and by the expulsion of the fetus. A physician who was summoned gave the patient chloroform, and said that he had removed the after-birth. On the following day she was admitted to hospital with normal pulse and temperature. The fundus of the uterus could be palpated just above the symphysis, the cervix admitted one finger, and there was no bleeding. Three days afterward, while straining, the patient felt as if a lump were coming down into the vagina, but she had no pain. On the following day, while straining after an enema, a red matted swelling appeared at the vulva. She was at once removed to the operating room and anesthetized. Upon examination, a protruding mass consisting of coils of small intestine matted together and covered with lymph was found. These were separated and the lymph peeled off. The tissues were thoroughly irrigated with salt solution. The intestine had come through the cervix, which was closing down upon them, and as the uterus seemed healthy they were replaced through the cervix and the uterine wall into the abdomen. A large tear was then felt across the fundus of the uterus. The patient was placed in the Fowler position, and the uterus, Douglas's pouch, and the vagina irrigated with salt

solution. The uterus and vagina were packed with sterile gauze, a large pad was placed over the vulva, and a T-shaped bandage applied. She apparently recovered without incident. Seven months afterward she returned, stating that she had suffered from abdominal pains like colic, chiefly in the right iliac fossa. Vomiting had developed with constipation, diarrhea, and emaciation. Upon examination, she was pale, anemic, thin, with subnormal temperature, and fairly good pulse. The abdomen was full but not distended, there was no rigidity, but slight tenderness in both iliac fossæ. The vagina, uterus, and rectum were normal, and enema returned clear. The patient passed flatus through the bowel, but vomited. At operation, extensive adhesions were present, and a piece of the iliac colon was found firmly adherent to the parietal peritoneum in the right lower abdomen. This was freed, and the raw surface on the bowel covered by peritoneum. Coils of small intestine were found adherent to the fundus, and, on separating this mass, the bowel was opened in two places. Upon examination, a proximal piece of the bowel was patent, but the lumen of the distal piece admitted only the tip of a pair of forceps. This constriction was divided, and end-to-end anastomosis made. Another loop of intestine was adherent to the bladder and was separated and repaired. The lower part of the wound was drained by a rubber tube. The patient made a good recovery.

Repeated rupture of the uterus within eleven months is reported by HEIL (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 3). The second accident was followed by death from septic infection. In each case the rupture was spontaneous.

A similar case is also reported by GOLDSCHMIDT (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 3) in a patient in her second pregnancy, who after her first labor suffered from septic infection. At the end of the second pregnancy she suddenly collapsed without having had genuine labor pains. She had, however, suffered from abdominal pain and from very strong fetal movements. The physician who first saw her diagnosed separation of the placenta, and the patient was brought in a motor car to hospital. There rupture of the uterus was diagnosed. On section a full term child was found in the abdomen, with free abdominal hemorrhage. The uterus had ruptured at the fundus and the placenta was adherent. Extirpation of the uterus and tubes was performed, the ovaries remaining. The recovery of the patient was uncomplicated.

BROADHEAD (*Amer. Jour. Obstet.*, April, 1912) reports the case of a patient, aged thirty-three years, a multipara, in whom the abdomen was pendulous, tense, and difficult to palpate. Labor pains persisted irregularly for five days, about three weeks before the expected termination of pregnancy. The membranes ruptured spontaneously. When the patient was seen, she was having no pains, and the cervix was not dilated. The head was not engaged, and it was stated that an unusual quantity of amniotic fluid had escaped. The patient was not seen again for several days, when dilatation was advanced sufficiently to admit one finger. The head was not engaged. Her physician supposed that she was in beginning labor, and left the patient, instructing her to send when pains developed. When next summoned, he found her in acute shock with the history of having

one severe pain, followed by complete cessation. The patient's night-dress was saturated with fresh blood, her abdomen was flaccid, and the fetus was easily made out in transverse position, the head to the right and near the umbilicus. There was no presenting part at the superior strait. Upon vaginal examination, the cervix admitted one finger only, and two old scars were present in the cervix. The patient died before she could be transferred to hospital, and no autopsy could be obtained.

Repeated spontaneous rupture of the uterus is described by BECKER (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft 1 and 2). He has collected 27 cases of repeated spontaneous rupture from the literature of the subject, to which he adds his own. The patient was a primipara, aged twenty-two years, who had hemorrhage at the end of pregnancy, without dilatation of the cervix. When a physician was summoned, he found the membranes ruptured, the os two-thirds dilated, and the head firmly wedged in the pelvic cavity, and no uterine contraction. Two days later a consultant saw the patient, when septic infection had developed. Craniotomy was then done, and as the fetal body was removed bubbles of foul gas escaped from the uterus. On examining the uterus with the hand, a complete rupture transversely across the posterior wall was discovered, and the placenta had separated and was readily removed. The uterus contracted well and there was no hemorrhage. In view of her critical condition and her surroundings, she was treated by drainage with iodoform gauze. Although severely ill she gradually recovered. Six years later another pregnancy occurred, when the patient went to seven months, when fetal movements ceased, accompanied by hemorrhage. The cervix was closed; there was some irregular pain, which gradually ceased. The pulse was strong, and gas escaped from the intestine. The patient refused to enter the hospital. Symptoms of peritonitis with septic infection developed, and the patient was finally brought to hospital. Upon examination, diffuse peritonitis was present, and an effort was made to empty the uterus by combined version. This was accomplished without great difficulty, and a macerated fetus and placenta were removed. Upon examination a tear upon the left side of the uterus was found, through which the hands passed into a cavity at the site of the contracted uterine body, and in this cavity were coils of intestine. Section was performed, but the death of the patient followed. Upon examination, no evidence was present of the first rupture, as the uterus had been completely restored. The laceration had occurred at the site of the old rupture, and upon microscopic examination it was found that the muscular tissue of the uterus at that point had been replaced by connective tissue.

GYNECOLOGY

UNDER THE CHARGE OF

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Tuberculosis of the Cervix.—In view of the extreme rarity of this condition, it is quite remarkable that BENDER (*Rev. de Gyn. et de Chir. Abdom.*, 1914, xxii, 29) should have had the opportunity of observing 2 cases within a short space of time. In the first case he did not suspect the true nature of the condition at the time of operation, which consisted merely in amputation of the cervix for a supposed mild-grade cervical metritis; histological examination of the tissue showed, however, the presence of typical tuberculous changes. A short time after this, Bender had occasion to operate upon a woman, aged thirty-four years, who applied for treatment on account of a mucopurulent leucorrhœal discharge, associated with dull pains in the lumbar region. She had had three healthy children, and one miscarriage, the latter about nine months before coming under observation. On examination, the cervix appeared large and indurated; the surface was granular, and somewhat friable, bleeding easily upon palpation. The appearance was not characteristic of cancer, and yet it was obviously not a simple cervicitis, so that a suspicion of tuberculosis was aroused in Bender's mind—a suspicion which was confirmed by histological examination of a small bit of tissue excised under local anesthesia. The patient's general condition was excellent, nothing suggestive of tuberculosis elsewhere in the body being discoverable. In view of the excellent results which had followed the simple trachelectomy in the former case, Bender deliberately chose the same conservative procedure in this instance, first, however, dilating the cervix and making a thorough digital exploration of the interior of the uterus, to assure himself that there were no gross evidences of its involvement. The cavity was then curetted, and swabbed out with iodine, the cervix being then amputated in the ordinary manner. Histological examination of the tissue showed typical tubercles, with caseation, and giant-cell formation; in slides stained for tubercle bacilli, these were found in considerable numbers. Notwithstanding that over two years have now passed since these operations, both patients are well, and show not the least sign of recurrence. Bender thinks, therefore, that in these, evidently early cases, with no sign of involvement beyond the limits of the cervix proper, he was justified in doing the conservative operation, though he does not wish to be understood as meaning to imply that this will suffice for all cases of tuberculosis of the uterine cervix.

The Role of Tuberculosis in the Production of Cystic Neoplasms.—In conjunction with the article, reviewed last month, by Pollosson and Violet upon tuberculosis as an unsuspected factor in the produc-

tion of ovarian cysts, a discussion of the same general subject by PONCET and LERICHE (*Lyon Chirurgical*, 1914, xi, 1) is of considerable interest. These authors state that in 1906 they propounded the theory that many apparent tumors are, in fact, nothing but neoplastic structures, which have developed as the result of some mechanical, toxic, or infectious irritant, expressing at the same time the belief that among the latter group, tuberculosis plays an important role. They now state that they have become even more firmly convinced that tuberculosis is the great cause of benign cystic neoplasms in various parts of the body. They have already demonstrated this with regard to cystic adenomas of the thyroid, and now wish to call attention to the frequency with which cystic ovarian tumors, not specifically tuberculous, are found in conjunction with tuberculous tubes. They report an example of this condition occurring in a woman, aged thirty years, in whom a large cystic ovary, and a microcystic oöphoritis were found in conjunction with a frank tubal tuberculosis, a state of affairs exactly analogous to some of those published by Pollosson and Violet. Poncet and Leriche ask, "Is it not rational to conclude, that in the presence of the same infection the tissues may react differently, the ovary being inherently very refractive to a frank tuberculous invasion, but very prone to neoplastic changes?" They do not mean to imply for a moment, however, that all simple ovarian cysts are of tuberculous origin, but merely to call attention to the fact that this is one cause that is often unrecognized.

Cysts of the Cervix Uteri.—There are two kinds of cystic structures which may occur in the region of the cervix, cystic tumors (*i. e.*, cystic degeneration of fibromata, sarcomata, etc.), and true cysts, which develop independently of any other uterine affection. Although the latter are exceedingly rare, DAMBRIN (*Arch. mens. d'Obst. et de Gyn.*, 1914, iii, 41) is able to report 2 cases that have recently come under his observation. The first case occurred in a multipara, aged forty-five years, who applied for relief from a mass which she herself noticed in the vagina, and which appeared at the vulvar orifice. On examination, an elliptical, smooth, bluish-gray, somewhat elastic feeling tumor, about the size of a hen's egg, was found attached to the posterior lip of the cervix by a pedicle as thick as the little finger. It was removed under local anesthesia, by cutting completely around the base of the pedicle. On opening the cyst, a second, smaller one was found within. Microscopic examination showed the walls to be composed of fibrous tissue, with a few scattered muscle fibres; it was covered externally by stratified squamous epithelium, the cyst cavity, however, being lined by a single layer of columnar cells. Throughout the fibromuscular wall were numerous glands of the cervical type, surrounded by areas of inflammation; some of these glands showed a distinct tendency to cystic dilatation. The second case occurred in a patient, aged thirty-two years, who had suffered with a prolapse of the uterus ever since the birth of her only child, six years previously. This patient also noticed herself a smooth tumor mass in the vagina. Examination revealed the presence of a rounded, conical-shaped tumor, the size of one's fist, projecting from the vulva. It was covered by vaginal mucosa, which appeared normal, except that the rugæ had

been smoothed out from stretching. Posteriorly, the cyst was attached to the anterior lip of the cervix, but anteriorly it was so intimately associated with the anterior vaginal wall that its exact delimitation was impossible. At operation, no plane of cleavage could be found here, and it was necessary to resort to sharp dissection with scissors in order to free the cyst, during which process it was ruptured, with the discharge of a quantity of blackish, tar-like material. A portion of the cervical lip was excised with the posterior portion of the cyst wall. The walls of the cyst were about 2 mm. thick, and were covered on the external surface by vaginal mucosa; the lining of the cyst cavity in this instance, however, was composed likewise of stratified squamous epithelium, no cells of the columnar type being found anywhere. Dambrin considers that all true cysts of the cervix may be divided into two groups: (1) Mucous cysts, of inflammatory origin, arising from the normal cervical glands as a result of obliteration of their outlet, and being, therefore, entirely analogous to the small, exceedingly common "ovula Nabothii." (2) Cysts arising from epithelial remains of embryonal structures in the uterine wall. Both remains of the Wolffian system (Gärtner's duct), and of the Müllerian ducts come into consideration here, the former much more frequently than the latter, however. In the case of cysts lined by *squamous* epithelium, such as the second specimen described by Dambrin, he considers the origin from Müllerian remains beyond question, but where the cyst is lined by *cylindrical* epithelium, as in his first case, the problem becomes more difficult. If the cells are definitely ciliated, or if a fairly definite muscle layer surrounds the cyst cavity, an embryonic (Wolffian) nature may be assumed, but where these characteristics are absent, the diagnosis from a mucous cyst, of inflammatory nature, may be exceedingly difficult or impossible. Such is the situation with regard to the first case reported, though Dambrin is inclined to place it in the inflammatory rather than in the embryonal group.

HYGIENE AND PUBLIC HEALTH

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Experimental Berberi.—WELLMAN and BASS (*Amer. Jour. Tropical Diseases and Preventative Medicine*, August, 1913, i, No. 2, p. 129). report a series of experiments to determine what common articles of diet other than rice will cause polyneuritis in fowls, and especially to ascertain whether the glucose and talc found on commercial polished rice, as milled in local mills, is the cause of polyneuritis. They found that in chickens fed exclusively on polished rice, *ad libitum*, the average daily consumption of glucose was 0.125 grams per day and of talc

0.0625 grams per day. It was found that when glucose was fed in amounts fifty times as much as a fowl would get in an exclusive diet of polished rice, and talc in amounts one hundred times as much, that neither will produce polyneuritis in fowls. It was then found that the glucose and talc, added in large amounts to rice polish, in no way prevents the cure of polyneuritis. The various foodstuffs used by Wellman and Bass in their experiments and the number of days it took to produce a polyneuritis follows: Sago, 20½ days; boiled white potato, 24½ days; boiled milled rice, 27 days; corn starch, 32 days; milled rice, 33 days; wheat flour, 34 days; corn grits, 36½ days; boiled sweet potato, 38 days; cream of wheat, 39 days; puffed rice, 39½ days; macaroni, 40½ days. As a result of their work Wellman and Bass conclude as follows: (1) Glucose and talc, when fed together or separately do not produce *polyneuritis gallinarum* in birds receiving a diet which does not itself produce the disease. (2) Glucose and talc in large amounts do not prevent prompt recovery from *polyneuritis gallinarum*. (3) *Polyneuritis gallinarum* can be produced by feeding milled rice and many other food substances which have neither glucose or talc on them. (4) Glucose and talc, therefore, play no part in the production of *polyneuritis gallinarum* which results from an exclusive diet of polished rice. (5) These experiments indicate that legislation or regulations against the sale of polished rice, based upon the fact that *polyneuritis gallinarum* results from feeding it as an exclusive diet, are not warranted. (6) The evidence here presented indicates that several other common articles of diet produce *polyneuritis gallinarum* as certainly as does rice, either polished or unpolished: in three instances these other foods produced the disease in quicker time than did rice. (7) There is, therefore, more argument against the sale of these common articles of diet, sago, Irish potatoes, and corn starch, than there is against the sale of rice, "polished" or "unpolished" milled or under-milled.

Perineal Abscess in a Typhoid Bacillus Carrier.—L. LEVY (*Deutsche medicinische Wochenschrift*, July 31, 1913) reports on the original illness of a patient which occurred at the age of fifteen in January, 1907. The patient remained in the hospital until August of the same year and was then discharged as a bacillus carrier inasmuch as the urine contained constantly typhoid bacilli. During the ensuing years the patient suffered considerable from urinary difficulties, and in 1911 he was refused enlistment in the army because of a purulent discharge from the urethra. In September, 1912, he was admitted to the hospital because of perineal abscess which, upon being opened, discharge thick, creamy pus containing typhoid bacilli in pure culture. The pus cavity connected directly with the urinary passage. The persisting urinary fistula was corrected by operation in February, 1913. The treatment of this case had been undertaken a number of times with urotropin but without result. That this man had been a serious cause of illness for those brought in contact with him is shown by the fact that in 1907, 9 of his associates came down with the disease; in 1908, 6 persons; in 1909, 4 persons; in 1910, 27 persons, and in 1911, 1 person.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Effect of Salvarsan on the Circulatory and Renal Systems.—

ALVERENS (*Arch. f. exper. Path.*, 1913, Band lxxii) conducted experiments upon rabbits, and found that long-continued administration of salvarsan intravenously brought about a slight nephritis attributable to the arsenic contained. In the toxic doses, administered during a short time, marked fall of blood pressure and serious interference with renal function occurred, but lesions were not visible in the kidneys. If neosalvarsan were administered for a long period, nephritis was not clinically observed, although definite change could be demonstrated in the kidneys. If administered for a short time, the giving of neosalvarsan was less deleterious to the animals than salvarsan. If nephritis had been previously excited by cantharidin, rabbits showed marked sensitization to salvarsan, whereas if the nephritis had been caused by mercury or chromic salts, that is, were essentially tubular, no ill results were obtained till large doses were employed. Animals with aortic and tricuspid incompetence were treated, with the result that cases of tricuspid insufficiency with resulting congestion of the abdominal organs bore salvarsan worse than those affected merely by an aortic leakage.

Thrombosis in the Lymphatic Channels.—OPIE (*Jour. Med. Research*, October, 1913) details some interesting observations upon thrombosis and occlusion of lymphatics. Opie points out that in circulating blood, the blood platelets perform an important part by gathering at the site of an injury to the endothelium, so that fibrin is deposited upon the mass of platelets. Lymph from the thoracic ducts, on the other hand, coagulates very slowly because of the small quantity of thrombokinase present in it; the addition of blood or of lymph-tissue-extract brings about firm coagulation. There is thrombin present, but thrombokinase is deficient. It was thought likely that thrombosis might be produced by direct introduction of tissue-extract or tissue cells into the lymphatics, and this was done after ligation of the thoracic duct near its point of entry to the venous system. Tissue cells or tissue juices introduced into the mesenteric lymphatics will then produce a prompt thrombosis. It was noticed that in such a state edema occurs, but that there was a marked tendency to rapid formation of collateral lymphatic circulation. Further, it was noted that if occlusion of the duct was produced, followed by injection of bacteria into the circulating blood, thrombosis in the lymphatics occurred. A necrosis of cells in contact with the lymph stream favors thrombosis in the lymphatic vessels, because in this way thrombokinase is brought into contact with the circulating lymph. Bacteria

are potent in bringing about this effect, doubtless because they cause injury of the endothelial cells, and the suggestion is made that bacterial infection is successfully resisted partly by reason of a free flow of lymph which is rich in bactericidal substance. If the thoracic duct be occluded, or in fact any large lymphatic trunk, edema occurs which is relieved by the establishment of collateral circulation. In the experiments above mentioned, this was brought about in one case by formation of a new channel which entered the proximal part of the ligatured duct, and in another case by collaterals which ran to the right thoracic duct; while in some cases no such communication could be made out, but the edema was not widely spread. If occlusion of the thoracic duct and injury of the mesenteric duct be produced, chylous ascites may occur.

Palæopathology.—PROF. RUFFER (*Jour. Path. and Bact.*, October, 1913, xviii, No. 2) has coined this unusual word to embrace knowledge that may be gained as to the inroads of disease upon bodies preserved to us from ancient times. He has had an opportunity of studying the pathological lesions in Coptic bodies dating from the fifth century of the Christian era. The bodies were not mummies in the proper sense of the word, but owed their wonderful preservation to the dry sand and to salt. They were evidently for the most part Christians, and many were dressed in embroidered garments. The teeth were found very badly diseased; caries was common; pyorrhea alveolaris and periodontitis were frequent, and it is evident that little care was bestowed in life upon the teeth by the Copts; nor was there any evidence that dentistry was understood by them. Spondylitis deformans was frequent, usually localized to a few vertebræ. Hypertrophy of the middle turbinated bones was noted; enlarged spleens, supposed to indicate malaria, were also found. The histological observations will be given later.

Tubercle Bacilli in the Feces.—So much has been written about the presence of acid-fast bacilli in the feces of tuberculous and non-tuberculous persons, that it is a little difficult for the casual observer to know what he should believe with regard to the frequent presence of tubercle bacilli in the stools. LAIRD, KITE, and STEWART (*Jour. Med. Research*, October, 1913) have undertaken careful experimentation with a view to clearing up this vexed subject. Many observers have shown the presence of tubercle bacilli in the stools of tuberculous people. By some this has been credited to swallowing the sputum, and by others to the presence of ulcers in the bowels. Many acid-fast bacilli in the stools of animals and of human beings ill with various diseases have been reported, and in some cases it has been definitely stated that these were tubercle bacilli. Tubercle bacilli are sometimes found in the stools, while none can be demonstrated in the sputum, while in a large series of cases with bacilli in the sputum they were also capable of demonstration in the stools. A series of cases was reported in which tubercle bacilli were found in the stools of all of 100 patients who had tubercle bacilli in the sputum, and in more than 20 per cent. of 1000 other persons. The above mentioned authors at Saranac have examined a large number of persons, and have concluded that nearly all patients with tubercle bacilli in their sputum

also have tubercle bacilli in the feces; whereas very few persons who have no tubercle bacilli in the sputum have even acid-fast bacilli in the feces. In most cases where acid-fast bacilli appear in the sputum animal experimentation was performed with positive results; the feces which did not contain acid-fast bacilli were frequently examined by experimental inoculation of animals with negative results. The authors did not find acid-fast bacilli to any marked extent in the feces of those whose sputum did not contain tubercle bacilli, and their conclusion is that sputum frequently swallowed during sleep is the most likely explanation of the presence of these germs in the stools. The authors further go upon record as doubting the frequent presence of tubercle bacilli in the blood, a position which is the more tenable because good workers have repeatedly failed to obtain them from the blood.

The Bacteriology of Condensed Milk.—ANDREWES (*Jour. Path. and Bact.*, 1913, vol. xviii, No. 2) has examined a large series of samples of condensed milk with regard to bacterial content, a study which gains some importance when one considers that 50,000 tons of this product are imported into Great Britain in a year. In spite of the "villainous appearance of the stained sediment," none of the samples could be accused of containing pus; a high cell count with a percentage of polymorphs of over ninety ought to be present before the presence of pus could be determined. As to bacteria, the process of condensation appears, in many cases, to sterilize the milk, but a notable exception is in the case of staphylococcus, which finds in sweetened condensed milk, a medium that is almost differential. Andrewes does not absolutely condemn a milk that contains 250,000 cocci per cubic centimeter; nevertheless he thinks it would be safer to do so, and that efficient pasteurization should be performed before the milk is condensed and sweetened.

Arterial Lesions in Rheumatic Fever.—OSKAR KLOTZ (*Jour. Path. and Bact.*, October, 1913, vol. xviii, No. 2) has studied an interesting case of aneurysm of the ascending aorta found in a boy, aged six years, with rheumatic fever. It was evident during life that the heart was seriously involved, and blood cultures gave a pure growth of streptococcus in short chains. In addition to the disease of the mitral and aortic valves, and much fibrinous deposit in the vicinity of the aortic opening, there was found in the ascending aorta, on the posterior surface, an aneurysm measuring $2\frac{1}{2} \times 2 \times 1\frac{1}{2}$ cm. Two-thirds of the circumference of the aorta was involved in this dilatation. Histological examination of the aortic wall showed that the external coat especially in the vicinity of the vasa vasorum were markedly affected. Infiltration was partly leukocytic and partly lymphocytic, and plasma cells were present. Nothing like abscess formation was found anywhere, but marked necrosis was observed in the areas of the muscular elements. In the sac, the adventitia and a small portion of media were reinforced externally by the pericardium. Fibrinous clot and its contained leukocytes were found in the interior of the sac. Streptococci were demonstrable in the affected tissues. The finding of so marked an arterial change in the course of rheumatic fever comes to us as a surprise, and yet there is no inherent reason why this should

be so. The development of aneurysm in rheumatic fever is like the process in syphilis, insofar as the inflammatory invasion begins in the vasa vasorum of the media and in the adventitia. The secondary intimal reaction with nodular thickening familiar in syphilis was not present. The reason that the bacterial invasion attacks the ascending aorta is as yet unexplained, but it is evident that the process is embolic, and is connected with the vasa vasorum in which fairly large masses of bacteria are lodged. Observations with reference to the effect of rheumatic fever upon the vessels come almost entirely from French literature, where for many years one has been able to find scattered reports. It would be well if closer observations were made with reference to the effect of such acute bacterial disease upon the arteries.

Anthracosis.—HAYTHORN (*Jour. Med. Research*, December, 1913, vol. xxix, No. 2) has published some interesting studies upon anthracosis, and the importance of this lesion on the course of other diseases. Contrary to general supposition, Haythorn finds that the upper air passages do not seem to be the portal of entry, for the epithelial layers do not appear to be invaded by soot particles. When carbon pigment in abundance was brought in contact with the mucosa of the mouth and upper air passages, he found no evidence of phagocytosis of such pigment higher than the lung alveoli. Large mononuclear cells are found in the alveoli, laden with pigment, or they may be found in the interalveolar or other lymph spaces. If pigment cells are seen in the deep layers of the bronchial mucosa, they are usually perivascular in position. Lymph channels of small and moderate size are often seen to be plugged by such cells, and there is ptosis, apparently out of proportion, great in amount. Haythorn thinks the pigment-containing cell is not the lining cell of the alveolus, but is an endothelial cell, and, as such, is perhaps identical with the endothelial leukocyte of the blood. Experiments showed that the polynuclear leukocytes are unimportant as pigment phagocytes. Haythorn further thinks that pigment once ingested remains in the cell until disintegration frees it. The phagocytic cells wander into the lymph channels, and lodging there, may become surrounded by connective tissue. The importance of the process rests upon the frequent lymphatic obstruction that results, which is favorable to the localization of a tuberculous focus, and unfavorable to the resolution of a pneumonic area. The pigment-carrying cells appear to take their part in the formation of a tubercle, and the presence of pigment does not preclude the ingestion and phagocytosis of tubercle bacilli.

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ORIGINAL ARTICLES

MEDICAL DIAGNOSIS IN RELATION TO SURGERY.¹

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THE domain of surgery has been so widened in our own time that there is scarcely a medical condition that may not in some of its phases become a surgical one. By the very vastness of his field has the surgeon been forced to specialize and to devote himself exclusively to the eye, the ear, the nose and throat, the genito-urinary tract, or the female genital organs. The advantages of such a distributive process are many—and are too well known to be reiterated here. But there are some incidental disadvantages. At first sight these might seem to have nothing to do with my present theme. There is, however, a very logical connection. We find that the laity no longer consult their family physician for their well-defined regional complaints—they go directly to the ophthalmologist, otologist, laryngologist, etc., who if he finds an operative condition proceeds in the majority of cases to deal with it surgically. Not all will deem it necessary or important to have a medical examination made, a neglect that may jeopardize the patient's life.

Medical diagnosis to my mind involves not only the recognition of the existence of a surgical condition but also a careful study of the patient as a surgical risk. No surgical operation requiring anes-

¹ Paper read before the College of Physicians of Philadelphia as part of a symposium on The Relation of Medicine and Surgery. The paper also formed the basis of an address before the Springfield Academy of Medicine, Springfield, Mass.

thesia should be done without the approval of a medical man, based upon a thorough examination of the patient. Such an examination involves a study of the heart, the blood pressure, the temperature, the lungs, the kidneys, the blood, and the psychic and nervous systems. The results of his findings, in so far as they may affect the operation and its before- and after-treatment, the physician should communicate to the surgeon and together they should weigh the patient's status. But while I hold that no operation should be done without study of the case by a competent medical man, I also believe that no surgeon should ever operate solely on a medical man's opinion. He should on his own account study the case from the broadest aspect and arrive at an independent judgment. If the two men cannot agree, than a colleague of proper standing should be called as an arbiter. Cases will, of course, arise in which a determined surgeon, in sole charge of a patient, will operate with the whole faculty against him, or in which the medical man, having the patient's life primarily in his keeping, will refuse to consent to an operation that all the surgeons hold imperative. Such cases, however, do not alter the fact that the *modus operandi* I have sketched is, both for the patient and for the fair name of medicine, most desirable.

Coming now to the specific topic I have chosen, I am overwhelmed with the immensity of the subject of the medical diagnosis of conditions surgical. It appears to me of some advantage to have a working classification and to give to this a regional basis. A further advantage is obtainable by lopping off all consideration of things that are obvious. There are a number of conditions the surgical treatment of which does not admit of a difference of opinion—such as strangulated hernia, division of a large blood-vessel, fractures, dislocations, impaction of foreign bodies in the air passages—these need not detain us. Yet it might not be amiss to point out one or two possible errors in diagnosis. Thus I once saw a woman supposed to be suffering from neuritis of the brachial plexus in whom I discovered a dislocation of the humerus. And further, in a study of cervical rib made several years ago, I found that this condition may lead to the diagnosis of aneurysm of the subclavian artery and of neuritis. A correct diagnosis would render possible a cure by surgical means.

Beginning with the head, medical diagnosis concerns itself with such surgical and quasi-surgical conditions as fracture, tumor, abscess, and meningitis. In many respects the first is the most important, inasmuch as where alcoholism co-exists the fracture may be overlooked. Not a few young internes have made this grievous mistake and have perhaps sacrificed life, and incidentally brought discredit upon themselves and their hospital. I have always taught that no obviously alcoholic patient should be sent from the hospital if he presented one of two conditions—a very

rapid or an unnaturally slow pulse—the former might indicate a dangerous weakness of the circulation, the latter cerebral compression.

The medical diagnosis of tumor need not be discussed in detail. There is but one point I desire to emphasize, viz., that uremia may in every way simulate tumor of the brain and without the guiding hand of a clinician, a useless and probably fatal operation may be done.

Abscess of the brain most often springs from middle ear disease. As the history is not always definite and as the patient is not rarely seen in a stuporous state, the ears and mastoid processes should always be examined in every obscure "head case." A history of chronic ear trouble and intense uncontrollable headache should arouse suspicion of abscess.

Meningitis of the suppurative type is, thanks to Irving Haines, now being claimed, somewhat furtively as yet, by the surgeon as his domain. Hence the medical man must be prepared to diagnose it as early as possible. Intense headache, rigidity of the neck, Kernig's sign, the character of the spinal fluid after lumbar puncture, are the signs and symptoms leading to a correct diagnosis.

In the neck the principal disease to interest us is exophthalmic goiter. No disease is more easily recognized and yet he who does not see it at once may remain blind to it despite its obviousness until someone else points it out. The medical man is called upon to diagnose the disease, the cardinal symptoms of which are too well known to need mentioning here, and at the same time to determine whether the patient is in an operative state—assuming that an operation is contemplated. He will advise against immediate operation if the patient is highly thyrotoxic—has pronounced tachycardia, enlarged heart, slight fever, gastric symptoms, and psychic exaltation.

In the case of lymphatic enlargements in the neck, the physician has to determine whether they are tuberculous, leukemic, or due to Hodgkin's disease. A blood examination will reveal the second, but is of little help in differentiating between the other two. The hard character of the enlargement and the presence of glandular masses elsewhere is in favor of Hodgkin's disease. It should also be remembered that spinal symptoms are sometimes an early manifestation both of Hodgkin's disease and of leukemia.

A word might be said about the status lymphaticus. If it can be proven that death in this condition is due to compression of the trachea by the enlarged thymus, then the medical man should know how to diagnose it speedily so that the surgeon may be called in time. The age of the patient, cyanosis, inspiratory dyspnea, dullness over the manubrium, and perhaps a laryngeal examination are aids to prompt diagnosis.

In the chest the diagnostic problems of surgical conditions are

few and not very troublesome. Most important is empyema. As far as its diagnosis is concerned, it should always be thought of in children suffering from fever with marked sweating and anemia. It should furthermore be borne in mind that it may be a terminal condition in the aged, manifesting itself only by fever and slight dyspnea. Between these extremes, a diagnosis is rendered somewhat easier if a history of preceding pneumonia is obtainable. There are, however, rare instances in which empyema seems to be there from the beginning. It then simulates pneumonia very closely. If the empyema is interlobar, the symptoms will suggest the presence of pus but the physical signs may fail to reveal its location. Localized tenderness may sometimes act as the divining rod.

If the medical man has located the pus by means of the exploring needle, the surgeon in operating should make his incision at the same place, no matter whether the spot is best from a surgical point of view or not. I have seen a surgeon disregard, for the purpose of getting better drainage, the point of puncture, and fail to find the pus. Sometimes with very marked symptoms only a spoonful of pus is present, and this may be missed if the surgeon does not follow the point of original entry.

When empyema has been diagnosed in an adult and the history reveals no previous chest condition, the possibility that the pus may be below the diaphragm should be envisaged. Depression of the liver dullness, a patch of tympany, data suggesting the existence of an old gastric ulcer or appendicitis, together with a radiographic examination will usually determine a subphrenic abscess. Exploratory puncture should be made with a needle of large calibre. It will demonstrate the presence of offensive "colon" pus and perhaps gas.

Abscess and gangrene of the lung are rare—diagnosis is far less difficult than localization. The x-ray is very helpful but may mislead us as to depth and height. The other signs and symptoms hardly need discussing.

The surgical conditions involving the heart are chiefly two—mediastinopericarditis and pericardial effusion. The operation for the former—cardiolysis—is still on trial, so that the medical diagnosis does not greatly interest the surgeon. Pericardial effusion is usually overlooked, more often, I think, than any other disease. The operation for paracentesis is done as often by the medical man as by the surgeon, but when the fluid is purulent the latter should be called in to establish drainage. I need not dwell on the diagnosis except to say that pericardial effusion may be mistaken for pneumonia. I have seen one case that might have been saved had the proper diagnosis been made.

A curious diagnostic error in connection with disease of the heart has come to my notice two or three times and as it has a surgical

interest I will cite one case. A patient had a large tender epigastric swelling, vomiting, anorexia, and great prostration. The surgeon to whom he had been referred diagnosed a gastric carcinoma, and decided to operate, but before doing so wanted a medical opinion. This opinion was "mitral stenosis, loss of compensation, enlargement of the left lobe of the liver, and congestion of the stomach."

In the diagnosis of surgical conditions of the abdomen, it is of practical advantage to treat separately what English and American writers call the *acute abdomen*. Many acute conditions are not grave and demand medical treatment only, such as indigestion, ptomaine poisoning, so-called, and lead colic. But a careful examination and a good history are always necessary or mistakes will be made. Assuming that the case is one of considerable severity—then, having ruled out a dietetic error as the cause, the first question should be: Is the trouble really in the abdomen or is it in the chest? A few months ago I was asked to see a man who was about to be placed on the table to be operated upon for appendicitis. The expert anesthetist, upon making a cursory examination, had grown a little suspicious of the heart and had demurred taking the responsibility of administering ether without the support of a medical opinion. Study of the case forced me to the conclusion that the man had lobar pneumonia and not appendicitis. The diagnosis was confirmed by subsequent events. This is not the only experience of the kind that I have had but in none did operation hover so close. I am inclined to think that too much stress is laid upon vomiting. If the initial chill of pneumonia follows hard upon a heavy meal, whether the patient is an adult or a child, vomiting is likely to occur.

Not only appendicitis but gall-stone colic, acute pancreatitis, perforation of a gastric or duodenal ulcer, may be simulated by chest conditions. Hence, before definitively diagnosing any one of these, the chest must be carefully explored. The laity, ignorant of the tribulations of the doctor, would never forgive an error in diagnosis that entailed an abdominal operation for a chest condition, but we who know how one may mimic the other, should be sparing in our criticism.

In the diagnosis of other conditions causing the acute abdomen, the history is of incontestable value. The age of the patient, previous attacks of pain and leukocytosis, may determine the diagnosis of appendicitis. It is indeed a fair assumption that acute inflammatory conditions of the abdomen during adolescence are of appendiceal origin, quite regardless of the area of greatest pain. I say quite regardless of the area of the greatest pain advisedly; the greatest *tenderness* is usually found on the right side.

In women the most important acute abdominal conditions to bear in mind, aside from appendicitis, are ruptured extra-uterine

pregnancy and torsion of an ovarian cyst. The former is not difficult of diagnosis. The history may help but does not always do so—pallor, sighing inspiration, abdominal dulness, and vaginal examination establish the diagnosis. Torsion of an ovarian cyst I have met four times. In none of the cases had there been any previous knowledge of the existence of the cyst or of any pelvic trouble whatever. Illustrative of the importance of medical diagnosis I may say that in the first case a diagnosis of uremia had been made by the attending physician on account of uncontrollable vomiting, there having been no other definite abdominal symptoms.

Acute conditions of the abdomen also rouse the suspicion of rupture of an ulcer of the stomach or of the duodenum. As prompt recognition is of the greatest importance, I will dwell for a moment on the diagnostic features of rupture in duodenal ulcer, as that is a fairly common happening.

Perforation of the ulcer is usually an extremely sudden process. It causes at once intense pain and collapse which may be followed in a little while by a temporary lull in the symptoms. This lull, which is probably caused by the non-irritant character of the duodenal contents, is very deceptive and may lead to errors in diagnosis. The pain is usually in the epigastrium but may be in the appendix region; the abdomen, until near the agonic period, is of board-like hardness. In the final diagnosis the history is of the greatest importance: a history of periods of disturbed digestion with pain (hunger pain), especially nocturnal, alternating with periods of good health. The male sex, as is now well known, predominates in duodenal ulcer.

Empyema of the gall-bladder may set in with acute or "stormy" symptoms, to use a Teutonic idiom, and may be diagnosed as ruptured gastric ulcer. The diagnostic points upon which I would lay stress are the history of previous attacks of colicky pain, good health in the intervals, tenderness in the gall-bladder region, and fever. Sometimes the gall-bladder can be felt if very light pressure with the warmed hand is made.

Another acute condition requiring a skilled medical diagnosis is acute pancreatitis. The symptoms of that are not characteristic. They may be interpreted as ruptured ulcer or empyema of the gall-bladder or intestinal obstruction. Perhaps the most valuable guide to correct diagnosis is to have pancreatitis in one's *arrière pensée*. Many difficult conditions, as Charcot remarked long ago, are happily diagnosed by merely thinking of them. If there is a history of gall-stones, the diagnosis of pancreatitis, if otherwise justified, is greatly strengthened.

A rather peculiar diagnostic difficulty came under my notice last year. A surgeon asked me to see an old lady suffering from intense pain in the right upper quadrant of the abdomen. It was doubtful whether the trouble was in the gall-bladder or in the

right kidney. Careful examination showed an erythema following the intercostal nerves and extending over the right upper abdomen. There were no vesicles but it seemed so much like herpes zoster that I ventured that diagnosis. Within a day or two the well-known vesiculation appeared. Dr. Lawrence Litchfield, of Pittsburg, has recently reported several similar cases.

I have not exhausted the acute abdominal diseases, but time does not permit me to include all of them. A word, however, about perforation in typhoid fever. Few conditions impose such a heavy responsibility upon the doctor. If he could be sure, his course would be easy, but the diagnosis is not as simple as some writers claim. A sudden pain, slight leukocytosis, rise in the pulse rate and of the temperature, and disappearance of the liver dulness are nearly sufficient for diagnosis and justify surgical intervention. All the symptoms, barring the last, may, however, be produced by suppuration of a mesenteric gland; but as this is also an operative condition, the possible confusion matters little.

Coming now to the consideration of more chronic conditions, we find one of the most difficult tasks to be the proper interpretation of the functional disturbances of digestion. Which are and which are not amenable to surgical treatment? Though the work of surgeons like the Mayos, Moynihan, Deaver, and Robson, has greatly clarified this subject, it still remains one of undoubted perplexity. The too enthusiastic abdominal surgeon, seeing some cases of dyspepsia and hyperchlorhydria associated with gastroduodenal ulceration, concludes that all such cases have a similar basis. I believe that hyperchlorhydria may be a purely functional condition. Even hunger pain and hyperchlorhydria are not infallible signs of duodenal ulcer. Yet, if the patient so suffering is a man and in every way a fit surgical risk, we are probably justified in advising an operation, on the assumption that the cause of his trouble is duodenal ulcer. The x-ray in skilful hands is of great diagnostic value, showing in these cases a hypermotility of the stomach with rapid propulsion of the bismuth meal into the duodenum. In every case of so-called gastric neurasthenia or nervous dyspepsia, characterized by bloating, eructation of gas, a variable appetite, and nervous depression, an organic basis should be suspected. Often it is gall-stones. A correct diagnosis is impossible without a careful history and a thorough physical examination, particularly search for Mayo Robson's tender point. We must not be misled by left-sided pain, for just as appendicitis may sometimes cause pain on the opposite side, so may gall-stones, especially when there are adhesions between the gall-bladder and the stomach.

As a matter of medico-surgical interest, I should not omit to mention the fact that the gastric crises of locomotor ataxia may closely simulate gall-stone colic.

The subject of splanchnoptosis is one of great interest at this

time. Its relation to chronic ill health and to constipation makes correct diagnosis and proper treatment a pious desideratum. I have not been convinced that surgery is the only way to success and believe that the admirable work of Coffey, of Portland, Maine, has demonstrated that much can be accomplished by purely non-operative means.

Abdominal tumors present great diagnostic difficulties, and the most skilled clinician often goes astray. Those involving the stomach are perhaps the least perplexing. Gastric symptoms of short duration, loss of weight, signs of food retention, and sub-acidity suggest carcinoma. Confirmation may be obtained by an x-ray examination. The position of the tumor is not of great moment. It may be anywhere from the right rectus to the left flank, from the epigastrium to below the umbilicus. Every effort should be made to diagnose malignant disease before a tumor appears so that removal can be accomplished before other parts near and distant are inseminated.

There is a type of tumor in the abdomen that gives rise to unusual diagnostic pangs. It may be found in the region of the colonic flexures on the left side and on the right side anywhere from Poupart's ligament to the border of the ribs. At first examination such a tumor may impress one as malignant if the patient has reached the cancer age, or as tuberculous if he is younger. Careful examination will, however, show certain peculiar features—the growth is rapid, there is usually a spot of great tenderness; there may be a periodic or continuous fever; and the blood count shows a leukocytosis. These signs, indicate, I believe, that the tumor is inflammatory, no matter how smooth or nodular, how small or large the growth may be. The mimicry of disease is never greater than in the case of these inflammatory swellings which have their origin in the appendix or in a diverticulitis of the colon.

The diagnosis of appendicitis is commonly so easy that the veriest tyro in medicine can make it. Difficulties arise in chronic cases, where the symptoms are chiefly those of dyspepsia and in certain acute cases in which the appendix occupies an abnormal position. In every case of dyspepsia in early adult life, the physician before incriminating the stomach or the nervous system, as is so often done, should carefully palpate the region of the appendix. Soreness when the colon is inflated with air and pain referred to the epigastrium on pressure at McBurney's point have recently been acclaimed as diagnostic signs of chronic appendicitis.

Intestinal obstruction is an important field in which prompt medical diagnosis with the aid of the surgeon often saves life. I shall not take your time to rehearse the symptoms of the various types of obstruction. Some, like strangulated hernia, are easily recognized if one makes it a practice in all cases to examine the hernial openings whether a hernia is visible or not. I want to

speak about two points only, first, that acute pancreatitis may simulate ileus and, second, that kaleidoscopic uremia may present the picture of intestinal obstruction.

With regard to the spleen, the condition of chief surgical interest is splenomegalic anemia, splenogenous cirrhosis of the liver, or Banti's disease. Here it is the medical man's duty to establish a correct diagnosis, inasmuch as removal of the spleen is the approved and proper treatment. The diagnosis is based on enlargement of the spleen, on a history of hemorrhages from the nose or the stomach, on the presence of anemia with leukopenia and, in more advanced cases, on evidence of coexisting hepatic disease.

The surgical conditions involving the kidney give rise to pain in the loin and flank. If the trouble is inflammatory, whether intrarenal or extrarenal, there will be tenderness in the costo-iliac space. From the surgeon's standpoint the conditions demanding particularly accurate diagnosis are perirenal abscess and unilateral nephritis.² A microscopic and bacterioscopic examination of the urine will assist in the diagnosis. It should be borne in mind, as I have already mentioned, that herpes zoster may in its pre-eruptive state simulate these renal conditions.

One other condition needs mentioning here on account of the diagnostic problems it brings in its train, and that is Pott's disease. Pott's disease is never too old to cause trouble. For some unknown reason, the tubercle bacilli in the sheltered region of the spine seem to live forever. If an abscess forms it will travel downward and may then cause symptoms of great perplexity, intercostal neuralgia and thoracic aneurysm being some of the diagnoses I have seen made.

In the case of the extremities, the surgical conditions coming under the physician's ken are few. I have mentioned dislocation simulating neuritis. Perhaps the most important is osteomyelitis, which when near a joint is likely to be mistaken for articular rheumatism. In a child, persistent pain at or near one joint is almost never rheumatic in origin. Furthermore, it should be remembered that what may seem to be abscesses along the course of the bones may in young infants be blood extravasations the result of scurvy. A proper diagnosis by the medical man, based on a careful history of the case, may prevent a useless and hurtful operation.

An interesting condition of growing importance is thrombo-angeitis. This may be erroneously treated as rheumatism by the medical man, and, as in one case I have seen, as flat-foot by the surgeon.

I have not exhausted the surgical conditions which it may

² See paper by Riesman and Müller, "Acute Unilateral Nephritis, with Report of a Case," *Archives of Internal Medicine*, June, 1913.

become the medical man's duty to diagnose. I have tried to focus your attention upon those more difficult ones, borderland cases they might be called, in which keen medical diagnosis is necessary for the proper coöperation with the surgeon, a coöperation he should not only be glad to accept, but eager to seek.

I would emphasize once more the value of a medical examination, not only in obscure but also in plain, simple surgical cases. The physician might find diabetes, nephritis, grave anemia, bronchitis, or serious heart disease, anyone of which would influence the surgeon in his work. Many delayed deaths after operation might thus be averted. I also feel that in medical cases which may at any time assume a surgical aspect, the surgeon should be consulted long before an operation becomes imperative.

In order to increase his diagnostic skill, the physician should make it a rule to be present at all operations on cases that have come before him. Sir Berkeley Moynihan in England and Deaver in this country have found it necessary to remind us physicians of the value of the *autopsia in vivo*.

In closing, permit me to say that in all spheres of life, the best work is team work, and the best team for the cure of human ills is the great medical triumvirate—the laboratory man, the surgeon, and the sane, level-headed physician.

THE ASSOCIATION OF UTERINE GROWTHS WITH GOITRE; TYPICAL AND ATYPICAL EXOPHTHALMIC GOITRE.

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LET those who believe that medicine has made no progress during the last thirty years, remember that during that time we have learned all that we know today concerning the physiology and pathology of the ductless glands. No chapter in medicine is more important, none more promising, none has added more to human happiness, for it includes the introduction of organic extracts into medicine. But three decades have passed since Brücke announced to the medical world that "so far as the function of the thyroid is concerned, we have absolutely no hypothesis to offer." At the same time, Wittiche made the statement that "we know less of the functions of the thyroid and adrenals than of the spleen and thymus gland, and that we know almost nothing of the latter." Since that day the association of animal experimentation, clinical observation, pathological research, and therapeutics have developed knowledge, supplying data which are leading

both the physician and surgeon to conclusions which in practice prove rational and life-saving.

The dawn is breaking and we are beginning to understand more clearly than ever before the far-reaching influences of the internal secretions and their reciprocal relations, including their effect on the growth and functions of individual organs. The importance of these revelations the profession fully appreciates.

The relations of the thyroids and genitals have been recognized by the profession and lay world during all the ages. The change in the size of the thyroid after defloration led many tribes to measure the organ with a thread to decide upon the chastity of the bride, because of its increase after initial coitus. Catull's Epigram is based upon the demonstration:

"Non illam gentrix orienti luce revisens
Hesterno poterit collum circumdare filo."

Gothe's Epigram so fully quoted by Freund is based upon the same physiologic observation:

"Ach, mein Hals ist ein wenig
geschwollen, so sagte die Beste
Ängstlich . . . Stille, mein Kind,
still und vernehme das Wort.
Dich hat die Hand der Venus berührt,
sie duetet dir leise.
Dass sich das Korperehen bald, ach
unaufhaltsam verstellt."

Von Eiselberg's experiments prove the close relation of the thyroid and sexual organs; Bircher, Freund, Ullman, and others have fully corroborated his conclusions.

The behavior of the thyroid during puberty, menstruation, pregnancy, labor, and lactation argues in favor of its close relation to the uterus and its dependencies. Kocher has found after extensive thyroidectomy profuse metrorrhagia, and classifies this symptom as "metrorrhagia thyreopriva." He concludes that the quantitative reduction of the menses in such cases is a direct proof of improvement, and treats these cases with thyroidin. Lawson Tait recognized the relation of the thyroids to the uterus, for he held that all women with goitre showed a tendency to menorrhagia and uterine anomalies. There are cases in which during amenorrhea the thyroid gland enlarges, to retrograde with the established flow (Sloan, Ewald, Klokow).

Mendes de Leon, four weeks after myomectomy in one of his cases, described atrophy of the thyroid; the gland persisted, however and was still palpable several years later. Glaessner, in a case with multiple uterine myomas and fully developed Basedow's disease, observed marked improvement and retrogression during the climacteric. Fraenkel believes that he has succeeded in reducing

the size of the goitre in myomas treated with x-rays, and he believes that the improvement in these cases is due to the cessation of ovarian function. W. F. Freund's study of the literature of the subject proves that the older descriptions of Basedow's disease included symptoms of functional disturbances of the organs of generation in women, though the gynecological abnormalities were not fully described. He was the first to investigate their association more thoroughly than had been done before, and he reported that without exception he was able to demonstrate chronic atrophic parametritis in all of his cases of exophthalmic goitre. In 1899 Kleinwachter called attention anew to the frequency of menstrual anomalies and changes in the organs of generation with exophthalmic goitre, and included the corroborative evidence offered by Jenks, Foote, Pastroit, Porchet, and P. Müller. Amenorrhea was a frequent complication included in these clinical reports. Cheadle before Kleinwachter called attention to the atrophic changes of the genitalia with exophthalmic goitre. It has been noted that if the disease attacks girls before puberty they are likely to remain amenorrheic (Henoch and Hall, and Edwards). Improvement or cure has, as a rule, been followed by the establishing of normal menstruation.

Exophthalmic goitre developing during pregnancy is exceedingly rare; it has only occasionally happened that the complex was influenced by parturition; usually the symptoms persist. It may be concluded that these patients have, as a rule, been unfavorably influenced by pregnancy, and convalescence has been abnormally slow. In my series of cases patients with exophthalmic goitre, with or without uterine growths, have rarely conceived.

During pregnancy all symptoms are liable to be aggravated, particularly those referable to the nervous system.

So far as the influence of castration on the thyroid is concerned, it is impossible to conclude that exophthalmic goitre is either favorably or unfavorably influenced by such treatment. Mathieus reports a case in which exophthalmic goitre developed after the removal of the ovaries, while Blocq reports a case in which the disease was cured after double oöphorectomy.

The close relationship of exophthalmic goitre and sexual life is accented by the preponderance of the disease in women.

Buschan in 980 cases of exophthalmic goitre found 175 in men and 805 in women. Mannheim reports the proportion of men to women in his cases 1 to 8.2 per cent. The proportion in the cases which serve as the basis for this article is 1 to 9. Until we had our cases tabulated, the frequency of exophthalmic goitre in men had not impressed us forcibly.

The writer has made an analysis of 5370 cases of internal diseases, and found 186 cases, or 3.46 per cent. of goitre. Of this number, 89, or 1.66 per cent., were simple, uncomplicated goitre;

97, or 1.8 per cent.; were diagnosed as belonging to the class of exophthalmic goitre; of this number 55, or 1.2 per cent.; proved to be atypical exophthalmic goitre; 42, or 0.78 per cent. were typical in all symptoms of exophthalmic goitre; 15 per cent. of all the cases of goitre seen (186) included in 5370 cases of internal disease proved to be associated with uterine myoma or fibromyoma.

Since 1881 my clinical experiences have demonstrated the frequent association of thyroid perversion, often hyperthyroidea, including simple goitre and exophthalmic goitre, typical and atypical with uterine growths, fibroid and myomatous.

In 1879 a case of typical exophthalmic goitre came to my notice in which there was also a fibromyoma of the uterus, which latter gave rise to but few symptoms, and was accidentally discovered. In this case the severe Basedow's complex ran its course, uninfluenced by medicines in about two years. Every prominent symptom save the goitre disappeared. The myoma caused but little disturbance during many years, but after fifteen years, underwent cancerous degeneration, which killed the patient. There never was a return of a single symptom of exophthalmic goitre.

My early experiences with this and other cases led me to observe in all cases of goitre wherever possible the condition of the uterus. This study has justified me in teaching since 1881 what I have observed, that is, the unusual frequency of uterine growths with thyroid abnormalities, more particularly with the various forms of goitre, typical and atypical exophthalmic goitre.

In 1891 W. Freund called attention to the association of frequent thyroid change with uterine myoma. It was found that the enlargement of the thyroid was more pronounced, with growths containing a preponderance of connective tissue. This association is by no means accidental; there is a causal relation. The association of these lesions has remained practically unnoticed, and has almost entirely escaped the attention which it deserves. This is true because the internist, whose function it is to treat thyroid perversion, in the majority of his cases finds nothing in the history which leads to the uterus as a source of symptoms, while the gynecologist in his cases of uterine tumor, limits his investigation to the organs in which he is most interested, and either overlooks or fails to record in his histories the presence of goitre with associated symptoms. The subject is one of exceeding importance from a pathological and therapeutic point of view, and we present but a few histories in abstract to support our contentions.

The following history includes sensory symptoms, analgesia, thermo-anesthesia, the typical picture of syringomyelia, cystic ovary, uterine fibromyoma, goitre, acromegaly, granuloma, trophic changes, invasion of the sympathetic system, multiple cutaneous pigment deposits, fibroid growths, and urinary anomalies:

Mrs. X., Cortland, N. Y.; housewife; aged fifty-two years; weight, 242 pounds, normal weight, 150 pounds; five feet five and one-half inches in height; coffee and tea drinker; temperate; has two children, aged thirty-two and twenty-one years respectively. Consultation with Dr. Higgins. Seen on April 6, 1910. Family history shows father and mother both dead. Father was rheumatic; mother had neuritis. All members of the family are and have been decidedly rheumatic. One brother died of Bright's and heart disease. Patient had the usual diseases of childhood, otherwise well; never had an accident.

Twenty-one years before she had noticed a peculiar sensation, which she said was difficult to describe, in the index and middle finger of the right hand. At times this sensation was painful, extended into both arms, and finally both hands were more or less numb; there was occasionally cramping in the hands and arms.

Twelve years before the diagnosis of uterine fibroid was made; later it was found that she had a large ovarian cyst, with a fibroid uterus. Five years before the cyst, weighing 28 pounds, was removed, also the fibroid uterus. She menstruated but once after the operation. One year after the operation her right hand became analgesic and thermo-anesthetic. These sensory symptoms were less developed in the lower extremities. Soon there was the same loss to pain and to heat and cold in the left hand. She was forced to watch her fingers, because when near the stove, handling hot water or fire, she unconsciously burnt herself, and when using a knife would cut her fingers, which for several years had grown larger, with a persistence of the sensory symptoms. At the time of her first visit there was a large blister on the tip of her middle finger, resulting from a burn, of which she had no knowledge at the time of its receipt. At various times she had burned and cut almost all of her fingers.

Three years before the characteristic growth of acromegaly became noticeable. Her feet and hands seemed to run a race in their development with the small bones of her face, particularly her jaw and nose. All of her facial bones were enlarged; the upper jaw was retracted; the lower jaw was pushed forward, enormously thickened, and broadened. The teeth of the lower jaw were far in advance of the upper. There was characteristic broadening of the nose; prominence of the frontal bones, but moderate enlargement of the calvarium. The greater changes were in the small bones of the face, including the jaw, also in the hands and feet. The tongue seemed too large for the mouth. It was enormously thickened, broadened, and when protruded covered an unusually large area, and was three and one-half inches broad. Just back of the upper teeth, springing from the buccal mucosa, there was a large granuloma. Almost immediately after the operation a double goitre developed, larger on the right side than on the left, both

lobes presenting a prominence about the size of a grape-fruit. There was some scoliosis, with the characteristic hold of the head. There was a peculiar "catching," as she expressed it, of her fingers when she tried to close her hands, and as she released them a peculiar cracking sound was heard.

An error of refraction was corrected by glasses; the eye reflexes were normal; the patella tendon reflexes at the time of her first visit were absent; ankle-clonus was absent. The eyes seemed small because of the abnormal development of the orbit.

The urine analysis proved exceedingly interesting. Specific gravity, 1025; acid reaction; amber colored; peculiar, disagreeable odor; turbid deposit; faint trace of albumin by both tests; no sugar; urea, 1.6 per cent.; phosphates increased; no bile; chlorides normal; uric acid, 0.80 per mille; faint trace of indican. Under the microscope there was found abundant bacteria; pus cells in large numbers; large, squamous, epithelial cells; occasional red-blood corpuscles; few finely granular casts; some amorphous urates. Blood examination showed: hemoglobin, 80; red-blood cells, 4,000,000; white-blood cells, 8000; no pathological nor morphological change.

Perspiration was excessive and erratic. She was very much depressed; pulse, 88; respirations, 18; temperature, 98.2°; blood-pressure between 90 and 100 mm. Hg. (Systolic).

PHYSICAL EXAMINATION. Superficial examination of the body showed many pigment deposits; rough, dry skin; multiple, small fibromas. There was one fibroma directly under the skin which annoyed her exceedingly over the spine of the tenth or eleventh dorsal vertebra. There was a well-developed panniculus adiposus.

When seen on September 28 the cutaneous fibroid masses had grown. One on the back was pedunculated and we tied it. Heart was slightly dilated; there was no murmur; the arteries showed some thickening. There were no physical signs referable to any other organs. Her mental processes were quick; she was disheartened by her facial change and felt her condition keenly. At the time of her second visit, September 28, she thought she was somewhat better. This was due to the fact that she had lost weight and her face in consequence looked a little thinner. Her weight was 214 pounds. Her syringomyelic and acromegalic symptoms were unchanged. Her shoulders were painful. She was much less depressed than she was when first seen, and took a more hopeful view of her condition. Perspiration continued annoying. Her sensory symptoms remained limited to her hands and feet, analgesia and thermo-anesthesia. There never had been muscular atrophy. The rigidity, which had been noted by Raymond, Dejerine, and Redlich, seemed to be increasing. Her speech seemed guttural because of the enormous space occupied by her enlarged tongue.

At the time of her last visit the left patella tendon reflex was feebly present, the right was absent. There was a faint ankle-clonus; her eye reflexes were all sluggish.



Case of associated acromegalia, syringomyelia, goitre, ovarian cyst, multi. subcutaneous fibromata, etc.

RECAPITULATION. The sequence of symptoms and pathological changes in this case are unique and interesting.

1. The peculiar sensations experienced over twenty-one years in her right hand marked the beginning of what later developed into a pure syringomyelia.

2. The development of uterine fibroid and the ovarian cyst progressed independently of the first-named condition.

3. The operation five years before, necessitated by the enormous size of the cyst, gave impetus to further developmental anomalies.

4. The prompt development of analgesia, thermo-anesthesia, and rigidity, all without atrophy of muscles, marked the beginning of the onward march of syringomyelia.

5. The prompt development of the goitre after her surgical operation was stimulated unquestionably by the removal of the organs of generation.

6. The rapid changes of acromegaly.

7. The development of the granuloma.

8. The prompt appearance of pigment deposits; excessive and erratic perspiration; multiple cutaneous and subcutaneous fibromas, *pari passu* with the goitre, and the development of acromegaly.

9. The invasion of the kidneys, probably in a limited parenchymatous nephritis, with an unusually high uric-acid content of the urine, while the urea was comparatively low. With these conditions there was a gradually increasing arteriosclerosis.

There were a number of interesting features in connection with the subject under consideration which deserve to be mentioned with a study of my material. Goitre is increasing, and so are thyroid perversions in all civilized countries, a fact to which Breitner has recently called attention. Probably we make more thorough search because of our increased knowledge, and detect the atypical cases which were formerly overlooked; but this fact is not alone responsible for the increasing frequency.

Whatever the complications which we consider associated with goitre, typical or atypical exophthalmic goitre, we are promptly convinced of two further facts:

1. One, surprisingly prominent, proves that the disease is often self-limited; spontaneous recovery is not at all uncommon.

2. The subjective and objective manifestations prove the protean character of many goitres.

There is a decided tendency to disregard atypical cases of exophthalmic goitre, and they often remain unrecognized. Cautious, clinical study proves the frequency of what Stern has called Basedowoid cases. These are atypical, but they include a sufficient number of typical symptoms to justify the diagnosis of thyroid perversion. There are a large number of cases associated with distant changes in which there are but one or two symptoms of thyroid disturbance. These cases justify the conclusion that much of the ill health of the patient is due to perverted secretion.

A study of thyroid disease emphasizes the fact that there are periods of latency during which there are practically no symptoms save a goitre, large or small. These periods are followed by exacerbations, including positive symptoms of hyperthyroidea, and in some marked changes in the arterial tree.

While writing this paper we were called to see a case in consultation with Dr. Osgood, at Jordan, a classic example of acute hyperthyroidism and uterine myoma, in a woman, aged sixty-four years, who for years had goitre without subjective symptoms. She was the mother of six children; family history showed some tuberculous taint; her confinements were all normal. Her previous

history showed that she had erysipelas many years before. Had always been a hard-working woman.

Last fall, after a period of stress, which included excessive worry, it was noticed that an insignificant goitre, to which she had given but little attention during the many years of its existence, was becoming tense, somewhat tender, and seemed to cause some obstruction. At once she became tired, excessively nervous, and had annoying and uncontrollable palpitation. She grew progressively worse; the symptoms were all more or less aggravated when lying on her left side. Three weeks before she was awakened during the night with alarming tachycardia and cardiac irregularity. She was much frightened, and said she was "unable to control herself." Dr. Osgood saw her at this time, and found her in a precarious condition; her pulse was so rapid that it could scarcely be counted, with frequent intermissions and marked irregularity. The tachycardia ceased as suddenly as it commenced, but the heart continued irregular. Coincident with these explosive symptoms, followed by marked depression, the patient, who had never before experienced any abdominal inconvenience, complained of soreness and tenderness in the lower abdomen. Careful questioning proved that the goitre had increased in size during the previous eighteen months, and that the eyes had become more prominent than normal during the same period. She further volunteered the information that she felt "tired throughout her abdomen," and that during the eighteen months there had been considerable distress, to which she paid but little attention. She passed the menopause at fifty-five years without symptoms, and until the beginning of the increasing tenderness in the lower abdominal regions she had no knowledge of a pelvic abnormality. Her last child was born when she was forty-four years of age.

The leading features in this case, as expressed by the patient, were the painful abdominal conditions, marked tenderness, the symptoms referable to her heart, the goitre, tremor, excessive nervousness, and loss of weight, with marked Graefe and Moebius, the complex of symptoms of exophthalmic goitre.

When we saw her on April 20, 1913, the pulse was 130; systolic blood pressure, 170; diastolic, 100; pulse amplitude, 70; heart enlarged and dilated; systolic bruit heard over the entire precordium. Uterine examination showed the presence of an enlarged myomatous uterus, at least four times the normal size of the organ in a woman, aged sixty-four years.

We could reproduce this history a number of times with the rehearsal of cases equally typical, of suddenly developing thyroid perversion, with associated uterine growths, in patients who had gone to middle life and far beyond without subjective disturbances, in which the sudden onset of symptoms had entirely ungeared the patient.

We are fully convinced that whatever distant lesions were associated with thyroid enlargement, it may be positively assumed that in the presence of goitre, whatever the previous history may have been, symptoms may suddenly develop referable to such growth; some of these cases may lead to acute and serious cardiac insufficiency, in others to paroxysmal seizures, and in the third class of cases, to continuous symptoms of thyroid perversion.

We have previously referred to "perverted function" and "perversion." We think in the present state of our knowledge this is justified, for we are not yet possessed of knowledge which is positive in connection with thyroid abnormalities, and we need a "loop-hole" through which we may finally escape more gracefully and easier than if we were dogmatic in our statements and attributed all symptoms to hyperthyroidism.

The hereditary tendency in goitre and uterine myomas is often striking. We have two sets of cases of this combination of lesions, showing family tendencies which it might be well to report at this time. One series was found in a family of seven daughters, in which a number of aunts and cousins on the father's side had goitre. The mother of the seven daughters presented a negative history so far as goitre and uterine growth were concerned. Of the seven daughters, six had palpable uterine myomas, and five had had hysterectomies performed. Four of the six sisters had palpable and prominent goitres; one required thyroidectomy after hysterectomy.

One of these seven cases was seen in consultation by Friedrich Müller and Prof. Amman in Munich; there was an enormous uterine myoma with a large goitre of the mixed type. In this case both Müller and Amman recommended the removal of the uterus first: the careful watching of the thyroid to note the influence of the removal of the former upon the latter. Both believed that they had experiences which justified the conclusion that possibly the goitre might undergo some atrophy. Dr. Howard Kelly removed the uterus; cautious watch of the thyroid followed; the hysterectomy had absolutely no effect upon the thyroid mass; in fact, it seemed to stimulate its growth, and one year later, because of moderate pressure and slight exophthalmos, Dr. Tinker removed the enormous goitre successfully.

In the second series of cases we found two sisters, the daughters of a mother who had a large goitre, both suffering from typical exophthalmic goitre. In both the uterus was the size of a large grape-fruit, and was fibromyomatous.

The influence of the removal of the goitre upon the uterine mass so far as we have been able to conclude from a cautious observation of these and other cases during a considerable postoperative period has been practically negative. With Dr. Tinker, we have watched a number of cases during the past two years which have

chanced to consult both of us, and we have had abundant opportunity to note the influence of thyroid operations upon coincident uterine growths. In none of these has thyroidectomy or ligation of the thyroid artery shown the slightest influence on the size of the uterine growth or the symptoms dependent upon its presence. In one case in which Dr. Tinker ligated both thyroid arteries in which there had been profuse menstruation during a long period, in spite of improvement in the general condition and the heart, with increased ventricular strength, menorrhagia persists uninfluenced.

In some of our cases we have found multiple fibroid growths in various organs of the body. In one operated by Dr. Jacobson, in 1901, the primary growth associated with goitre was found to be innocent, about the size of an English walnut in the left vulvovaginal gland. Since that time this patient, who is now passing through the menopause, has developed, with persisting enlargement of the thyroid, acute exacerbations of symptoms, including paroxysmal tachycardia and enormous uterine myomas. She refuses operation.

In another case we have practically the same history, with multiple pigment deposits in the skin covering the thorax, abdomen, and a large crop of pedunculated cutaneous fibroids.

The symptoms dependent upon the uterine growth with thyroid enlargement are variable and not materially different from those associated with the uncomplicated cases. It is exceedingly difficult to determine the influence of the enlarged thyroid or hyperthyroidism upon the symptomatology of uterine growths because of the irregular behavior of the latter in the majority of uncomplicated cases. We think we are safe in concluding that in the presence of thyroid enlargement and uterine growths, operations on one of these organs does not materially influence the progress of the growth in the other nor the associated symptoms, save as the general condition of the patient is improved by the removal of an impediment and the source of toxemia. We are fully aware of the fact that this has not been the universal experience of clinicians, and that some surgeons have pointed, with a great deal of confidence, to the report of Wettergren's case, in which the removal of a submucous myoma favorably influenced Graves' disease.

A large number of uterine growths are associated with tachycardia and other circulatory anomalies. In some of these cases there is a palpable thyroid, in other cases there is no evident enlargement of the gland. In some an apparently normal thyroid may become tender and slightly enlarged during the presence of tachycardia. There may be localized tenderness, with slight enlargement of one lobe of the thyroid. In all of these cases we must investigate cautiously to determine the factor which has ungeared the circulatory system. In the presence of several of

the symptoms of hyperthyroidea or perverted functions and the absence of other causes, though there is no evident goitre, we favor strongly the thyreogenous origin of the tachycardia. This subject has recently been fully considered and the literature reviewed by von Jaschke.

The blood-pressure in cases of goitre associated with uterine growths is either normal, slightly elevated, in occasional cases only little reduced. Hyperthyroidea is not a hypotensive disease, neither can it be considered hypertensive. The revelations of the sphygmomanometer are often surprising, for with a thin, small pulse, a mere thread, uncontrolled tachycardia, often with ventricular dilatation, the blood-pressure shows no fall. This is a conservative measure of Nature.

It is the object of this paper to call the attention of the profession to the large proportion of uterine growths associated with goitre, typical and atypical exophthalmic goitre, to impress further the frequency of the atypical cases, and to encourage the thorough examination of all the organs of the body in the presence of goitre, large or small; if this be done, the number of associated anomalies will prove surprising.

A PECULIAR UNDESCRIBED DISEASE OF THE NERVES OF THE CAUDA EQUINA.¹

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WITH A PATHOLOGICAL REPORT.

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LESIONS of the conus and cauda equina give rise to symptoms easily recognizable; their precision is such as usually to make plain the topographical diagnosis of affections of these areas.

The characteristic symptom-complex consists in a paralysis of the bladder and rectum, a segmental palsy of the anterior tibial muscles of the lower motor neuron type resulting in drop-foot, with, in the majority of cases, a loss of sensibility in the affected root areas. In moderately complete cases this comprises a roughly semicircular area over one or both buttocks, corresponding to the

¹ Read at the meeting of the American Neurological Association, at Washington, May 5, 1913.

third, fourth, and fifth sacral root areas, a strip down the back of the thigh corresponding to the second sacral root area, with at times similar loss in the leg below the knee corresponding to the areas under the sensory control of the lower lumbar roots.

From conal lesions these symptoms are usually bilateral; from caudal lesions they may or may not be so, depending upon the type of morbid process at work.

A tumor lying on the roots and producing bilateral symptoms must of necessity be so large as to be aggressively obvious on inspection. If no tumor be found, there may be evidence of a meningomyelitis or of old disease of the bony spine, due to trauma, newgrowth, tuberculosis etc. If we cannot obtain such evidence from clinical and laboratory methods and from examinations on the operating table or in the postmortem room, we are compelled to hypothecate a more or less diffuse disease of the roots suggesting an infection or intoxication as a causative factor. And finally, if in cases of a certain clinical type we consistently find a characteristic lesion of the roots on the operating table, we are justified in concluding that that lesion is causative of the symptom-complex present.

During the past five years in a large number of spinal operations under our observation, 84 of which were performed by one of us, and among which were many cases of diseases of the terminal spinal segments, we have met with 5 cases so alike in their histories, in their clinical findings, and in the morbid appearances on the operating table that we have been led to class them together, in the belief that we have here a definite clinical and pathological entity.

CASE I.—Morris K., aged forty years, service of Dr. Collins at the New York Neurological Institute. Admitted May 27, 1910. Eighteen weeks before admission while bending down the patient felt a severe pain in the small of the back. The following day the pain in the back had disappeared, but he began to have pain in the right lower extremity. The pain came on in attacks, and extended down the thigh and leg to the ankle. It persisted off and on for four weeks, and then disappeared, to return with great severity a few days later. For ten days the pain in the leg disappeared, but there was a burning sensation over the right hip. The pain around the hip was severe enough to keep him in bed for three weeks before his admission to the hospital. For two weeks the right leg felt weak. On May 6 he was unable to pass his urine and had to be catheterized, and from then on he had great difficulty in urinating. For some time the patient noticed that he could not walk more than three or four blocks without getting tired. No symptoms were referable to the left leg. Bowels were markedly constipated.

The patient is married and has healthy children. He denied any syphilitic infection.

On examination he was found to be a strong, healthy-looking man. When he attempted to stand or walk it was evident that the right lower extremity was weaker than the left. The cranial nerves and the upper extremities were normal. Abdominal reflexes were lively and equal on both sides. The right lower extremity was slightly thinner than the left.

Knee-jerks were exaggerated on both sides; ankle-jerks could not be obtained; no clonus; plantar: right, extensor; left, flexor.

There was no rigidity or tenderness of the spine.

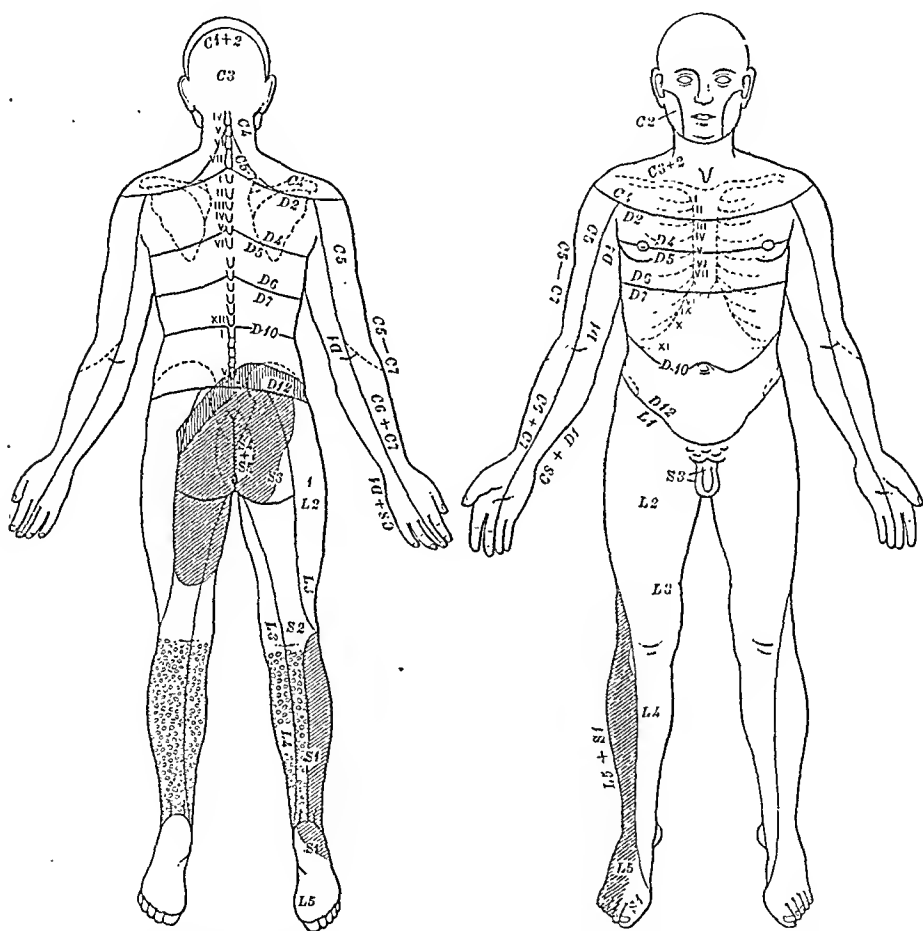


FIG. 1.—CASE I. Oblique shading, marked diminution of tactile and pain sense; verticals, hyperesthesia; circles, diminution of thermal sensibility.

There was a marked diminution of all sensations over the right side of the penis and scrotum, also over parts of the anal region, buttocks, and lower limbs (Fig. 1).

Wassermann test and x-rays were negative; urine was normal.

June 2. Laminectomy (Dr. Elsberg). Removal of spinous processes and laminae of the first, second, and third lumbar and later of the twelfth dorsal vertebræ. Bone normal; outer surface of dura normal, pulsating strongly. After incision of the dura, escape of a

large amount of cerebrospinal fluid. As soon as the dura was opened, several of the nerve roots were observed to be swollen and of a bluish-red color, contrasting markedly with the other roots of the cauda equina. It was not definitely determined *which* roots were affected, but four or five presented an abnormal appearance. Careful search in the spinal canal was made for a tumor, the nerve roots being lifted out of their bed so that the spinal canal could be well examined. The twelfth dorsal arch was removed and the dural incision extended upward so as fully to expose the conus. No neoplasm was found. The affected roots were thoroughly washed with warm saline solution, and the inner surface of the dura was examined and found smooth and glistening. Then followed suture of the dura, muscles, fascia, and skin in the usual manner.

June 10. Wound dressed, primary union, sutures removed; patient catheterized since operation.

June 20. Out of bed; general condition excellent; area of disturbed sensation on legs had disappeared; area on buttocks remained unchanged. Patient could flex and extend his spine freely; the pain in the back and right hip had disappeared entirely, so that he could walk around freely; could empty his bladder without difficulty.

June 29. Discharged; area of anesthesia over buttocks was still present; sensation over scrotum was normal. Patient declares that he felt perfectly well.

CASE II.—Mrs. St. J., aged thirty-seven years, married, no children, a patient of Dr. Brooks Wells and of Dr. Dana, through whose courtesy we report this case.

First seen on May 21, 1912. Two years before the patient had an attack of pain in the right thigh, shooting from the hip and lasting nine weeks. About one month later she had another slight attack of pain, and thereafter had some pain off and on up to the time of coming under observation. About eight months before she began to have pain in the small of her back and in her rectum. Later she was more than usually constipated. In January she had noticed that both lower limbs felt weak; had considerable pain in the left leg and numbness in both knees.

In April an abdominal hysterectomy was done, on account of difficulty with her bladder and rectum. She recovered satisfactorily from the operation, but her symptoms were unrelieved and steadily became worse. After operation she had retention of urine for three days, then she regained control of her bladder for two weeks; from that time on she lost all control of that organ and had to be catheterized. From May 14, she had severe shooting pain in the right leg and in the back, and noticed that her right leg felt stiff when she attempted to move it, and that she did not feel the catheter when the urine was withdrawn. Her bowels were constipated, excepting after a cathartic, when incontinence prevailed.

She was confined to bed for several weeks before our seeing her, on account of the pain and weakness of her lower limbs.

On examination the patient was a woman of small stature and slight build. Cranial nerves and upper extremities were normal.

Abdominal reflexes were present and equal.

Flexion of the right thigh at the hip and dorsi flexion of the right foot was weak. Knee-jerks were present and equal; ankle-jerks were present on the left, could not be obtained on the right side. The muscles of the right thigh were flabby. No loss of deep muscle sense in lower limbs.

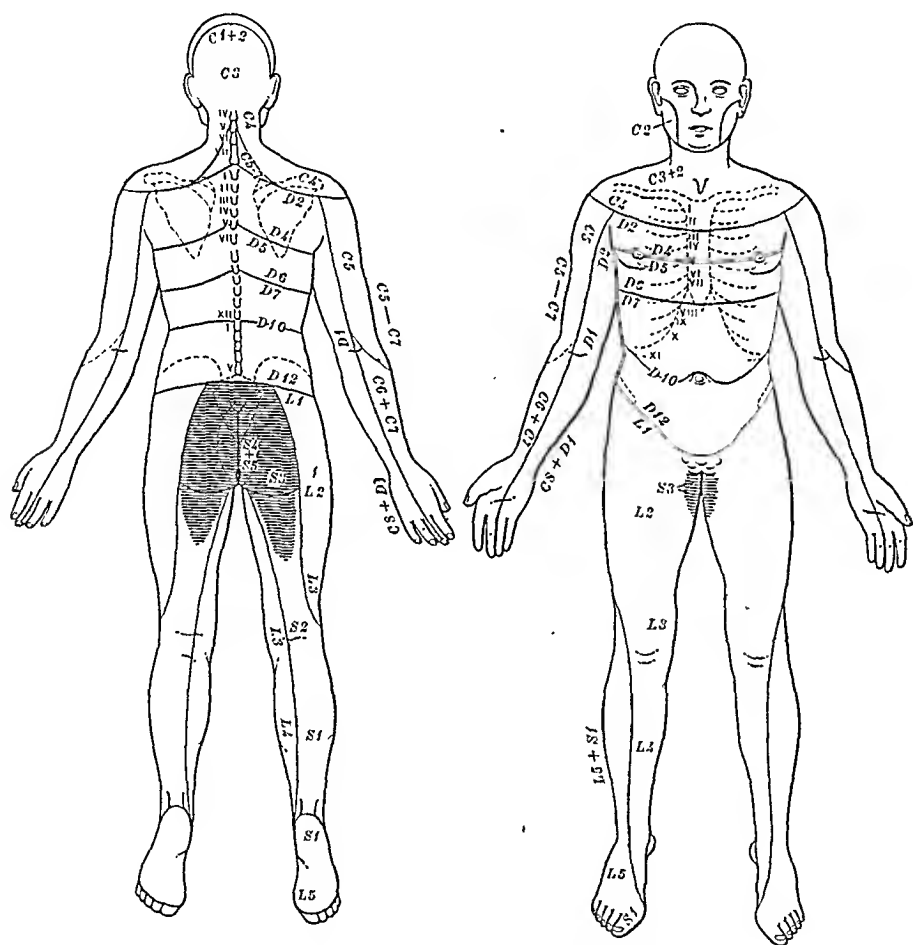


FIG. 2.—CASE II. Area of loss of all sensation.

At a second examination several days later, ankle-jerks on both sides could not be obtained; there was a loss of all sensation over the second, third, fourth and fifth sacral areas on both sides (Fig. 2). Wassermann test was negative; fluid obtained by lumbar puncture was of a light yellow color; globulin increased, 20 cells to the cubic millimeter; x-ray examination was negative.

June 18. Laminectomy (Dr. Elsberg). Removal of spinous pro-

cesses and laminae of the eleventh and twelfth dorsal, and the first, second, and third lumbar vertebrae in the usual manner; when the dura was incised, considerable fluid escaped, and the roots of the cauda equina were found deeply congested and of a reddish-blue color. Numerous tortuous vessels ran between the nerve roots. The inner surface of the dura showed a few small spots of congestion, but everywhere it was smooth and glistening. All sides of the nerves of the cauda, of the conus, and of the lumbosacral cord were examined, but no evidence of a tumor, of a bony abnormality, or other lesion could be found. A probe was passed upward and downward without meeting any obstruction. After the toilet of the wound, bichloride of mercury solution, 1 to 500 was rubbed on the nerve roots, and the dura, muscles, fascia, and skin closed in the usual manner. Duration of the operation, forty minutes.

Convalescence from the operation was uneventful; the wound healed by primary union.

June 26. For the past few days the patient had been able to feel when her bladder was distended. She once passed several drams of urine voluntarily. After taking a cathartic she still had incontinence of feces. Had not had any pain in her lower limbs since operation.

September 1. Had gained almost complete control of her rectum, and at times could pass urine voluntarily. Was free from all pain. Both ankle-jerks present, but weak.

February, 1913. General condition was excellent; had gained much flesh and strength. Passed urine without trouble, but had four to six ounces of residual urine, and had to be catheterized occasionally. She had considerable sensation when her bladder was distended and some urethral sensation had returned. Bowels moved well after small doses of cascara, and she was conscious of the desire to go to stool. Had occasional pain in her right leg. Knee-jerks were lively and equal; left ankle-jerk was lively, right was weak, but distinct. There were irregular areas of diminished sensation over the third, fourth, and fifth sacral areas, but they were indefinite, and their limits could not be mapped out. In some parts of these areas sensation was good while in others it was poor. Vulva was sensitive to touch and pain. Patient said she felt the catheter plainly when it was inserted and withdrawn. Could recognize the temperature of an enema, and declared that she was much better than when last seen.

CASE. III.—Elizabeth B., aged forty-five years, service of Dr. Peterson, at the Neurological Institute. "Sciatic rheumatism" in right hip for two years before admission, of about three months' duration. Soon after this the patient noticed that her right lower limb was becoming weaker, so that she dragged it after the other when walking. At about the same time she began to have pain in

her ankles, chiefly on the right side. The pain in the right hip returned at times, but gradually disappeared after about one year from the beginning of her trouble. From October, 1911, she had a recurrence of the pain about the right hip; thereafter it became steadily worse. At first the pain came on in attacks, but later it was continuous. From February, 1912, the right leg became much weaker. The pain in the ankle also reappeared, as did pain in the other ankle. For six months she had attacks of severe pain in the small of the back and became constipated. She had frequency of urination for many years before the onset of her symptoms.

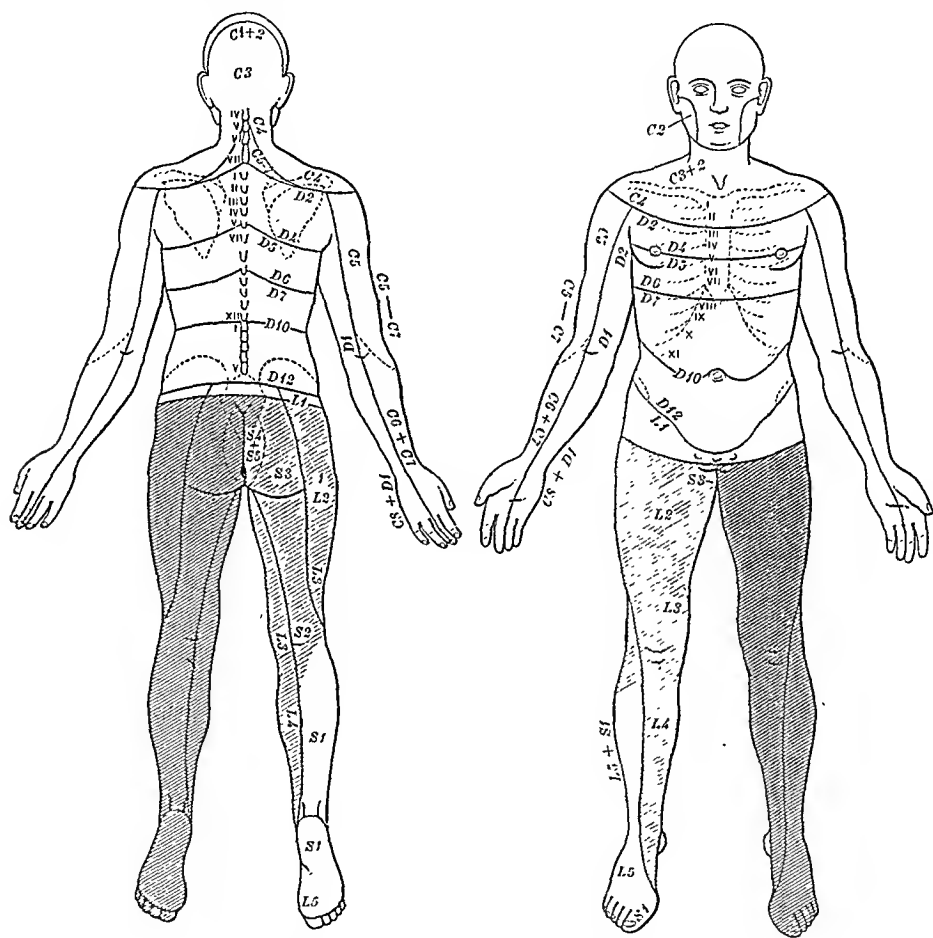


FIG. 3.—CASE III. Elizabeth B. Almost complete loss of all sensation; close shading, marked loss; wider shading, moderate loss

Physical Examination (May 27, 1912). General condition good; well-nourished; patient could walk only with great difficulty; she needed support on both sides. Both legs were spastic. Cranial nerves and upper extremities were normal. Abdominal reflexes, left upper and lower, were weak; right upper and lower could not be obtained.

Lower extremities: power fair at ankles on both sides; flexion

and extension at left hip and knee good; flexion at right hip and knee poor; the patient could raise both limbs from the bed, but the right always lagged behind the left. Both knee-jerks exaggerated; the right more than the left; both ankle-jerks were exaggerated and equal; double ankle-clonus, exhaustable on the left side; right plantar reflex extensor; Oppenheim sign on the right side; double paradoxical adductor reflexes were most marked on the right side when the left patellar tendon was tapped. No loss of deep muscle pain sense in lower extremities. The muscles on the outer side of the right thigh were tender to pressure.

For sensory disturbances see appended chart (Fig. 3).

The lumbar spine was held rigid; the spinous processes of the twelfth dorsal and first lumbar vertebrae were tender to pressure and the first lumbar spine was somewhat prominent.

x-ray examination was negative; Wassermann test was negative; no increase of cells or globulin in the cerebrospinal fluid obtained by lumbar puncture.

May 28. Laminectomy (Dr. Elsberg). Spinous processes and laminae of the eleventh and twelfth dorsal and of the first lumbar vertebrae and later of tenth dorsal removed. Dura was incised and considerable fluid allowed to escape. Cord pulsated well. Lumbo-sacral cord and conus covered by a fine network of congested vessels.

All the roots of the cauda equina were of a pinkish-blue color, unlike the normal color of the roots, and seemed to be covered by fine, congested vessels. Inner surface of the dura seemed to be congested in spots. Careful search was made for a tumor on all sides of the lumbosacral cord and conus and beneath the roots of the cauda equina, but nothing further abnormal was found. The nerve roots were thoroughly rubbed with sponges dipped in 1 to 500 bichloride of mercury solution, and the wound was closed in the usual manner.

Convalescence from the operation was uncomplicated.

June 7. The patient was up and about, and there was considerable improvement in her walking. Power in both limbs was fair, but the right was much weaker than the left. Both knee-jerks were still exaggerated, but the ankle-jerks were normal, without clonus. Double Oppenheim reflex. Sensory examination revealed some improvement.

June 28. Was able to walk around the ward without help. Power in both limbs was fair but the right was still weaker than the left. Both knee-jerks were exaggerated, the left more than the right. Both ankle-jerks were active; no clonus, Babinski sign and Oppenheim sign on right side. Spasticity in lower limbs was slight. Sensation in lower limbs (Fig. 4) was distinctly improved. It was impossible to find any definite loss of tactile sense, and the disturbance in the pain sense was indefinite, so that the examiner was often in doubt as to whether the pain sense was really disturbed. No

definite areas could be mapped out. Power in right limb was much improved. Patient could raise the right limb from the floor much better. To this fact she spontaneously referred.

July 12. Continued to improve, but complained at times of pain in the back. The spasticity of the right lower extremity was much less, and the power in the extremity was much greater.

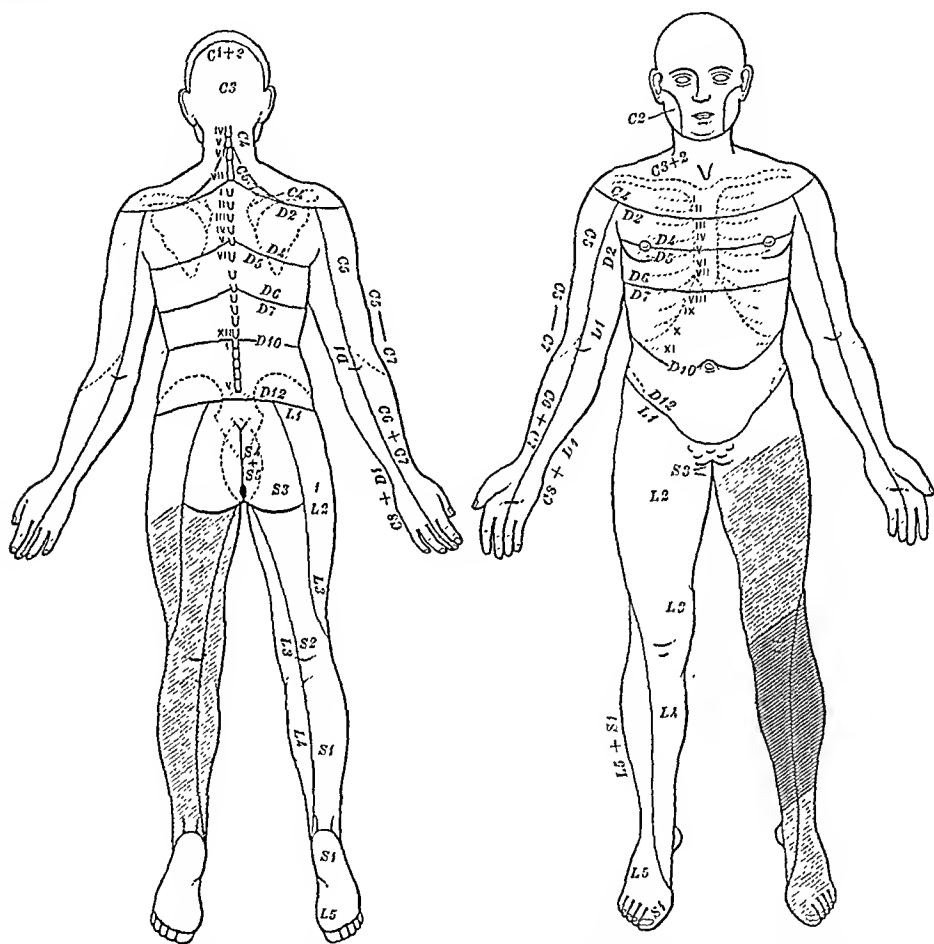


FIG. 4.—CASE III. Elizabeth B. Showing marked improvement four weeks after the operation. Compare with Fig. 3.

CASE IV.—Percy M., aged forty-four years, married, minister, service of Dr. Collins at the Neurological Institute.

The following history was obtained from his family physician, Dr. Vanderpoel Adriance: "In 1893 the patient had a fistula in ano, which was operated upon and the sphincter severed. He had suffered from nasal catarrh and inflammation of the left frontal sinus, for which he had been treated by irrigation and catheterization. Had had attacks of asthma and a number of attacks of so-called lumbago. Five years before while climbing in the Alps, he fell, striking upon the lower end of the spine; he suffered for several

days, but recovered without trouble. He thought nothing of the injury at the time, and recalled it only when questioned.

"Three years before, in the autumn, the patient came to this country, and while lifting a heavy article of furniture, felt a sharp pain in the back and down the back of the right leg. It had the distribution of "sciatic" pain. In December of that year, while skating, he fell heavily upon his back and had severe pain for several hours. After this injury the pain in the back of the leg appeared to have become worse. In March, 1910, that is, three months after the fall, he was sent to Dr. Goldthwaite, who made a diagnosis of right sacro-iliac strain, and applied a brace with a pad over the pubes and sacrum. At this time he was suffering from nervous depression, and this depression has remained ever since. Had a bad attack of asthma the following autumn.

"In the autumn of 1911, the patient, without apparent cause, had an attack of what appeared to be sciatica in the right limb. This was accompanied by numbness in the large toe and foot.

"In November, 1912, while getting out of his bath, he was rubbing his back with a bath towel, the ends being held in the hands, when the pain in the right leg suddenly returned. Since that time the pain has persisted, and at times shifts from the back of the right to that of the left leg. The patient was taken to New York, where an eminent orthopedist was consulted, and an x-ray taken. The bones in the lumbosacral region appeared normal on the plate."

The pain soon disappeared from the back but remained in the lower extremities, and he had a feeling of pins and needles in both feet and numbness in the buttocks. These symptoms persisted unchanged up to the time of his admission to the hospital.

November 17. Patient was in a much depressed mental state. Signs of old frontal sinusitis on the left side. Marked arcus senilis. Heart and lungs were negative; cranial nerves and upper extremities were normal.

Upper and lower abdominal reflexes were present and equal; cremasteric reflexes were present on both sides, but weak.

February 5, 1913. Patient complained only of pain caused by his cystitis, which had been severe in spite of frequent bladder irrigations. There was considerable atrophy of both lower extremities, more marked on the left side; complete foot-drop on both sides. The patient was able, with great effort, to flex each thigh on the abdomen to a slight extent, and he could weakly flex the legs on the thighs. All motor power was evidently much reduced. He was able to flex and extend the toes a little. He was not able to stand or walk.

Knee- and ankle-jerks absent; no plantar response. Abduction and adduction of the right thigh was weak; on the left side it was somewhat stronger. The limbs could be rotated outward fairly well, but inward rotation of the thighs was very poor.

the roots, as if an adhesion had existed at this point. Careful exploration failed to reveal a tumor within the spinal canal or any abnormality of the bony framework. A probe was passed upward within the dura for a considerable distance without meeting with any obstruction. The inner surface of the dura was everywhere smooth and glistening. The roots were thoroughly rubbed with bichloride of mercury solution, 1 to 500, followed by adrenalin solution, and the wound was then closed in the usual manner.

March 15. Wound healed by primary union; convalescence from operation was uneventful. The patient was much troubled by his bladder pain, but this was relieved by the insertion into the bladder of a permanent catheter. There was a slight contraction of the right quadriceps when the patellar tendon was tapped. The patient was able to be out of bed in a chair, and had been able a few times to pass urine in small quantities. He was able to control his movements.

April 24. For the past month the patient had been able at times to pass a fair amount of urine, voiding as much as six ounces at a time, with effort. He complained of pain in the bladder region. Cystoscopy showed that he still had a marked cystitis, with paralysis of the vesical neck. He was not certain if he had sensation in the bladder and rectum during urination and defecation. Abdominal reflexes were lively and equal; power in lower extremities was decidedly improved. He could raise both legs vertically from the bed, although the left was evidently weaker than the right. Flexion of thighs at the hip was good; flexor power at the knees was weak; the left was weaker than the right; extension at knees was strong; abduction of the thighs was weak; adduction was excellent. Double foot-drop persisted. Right knee-jerk was present and weak; left could not be obtained. Ankle-jerks were absent. Deep muscle pain sense was good in both lower limbs. Has not had any erections or sexual feeling for six months. The sensory disturbances were unchanged from those charted before the operation.²

CASE V.—F. K., aged thirty-seven years, was admitted on June 18, 1912, to the Cornell Medical Division of Bellevue Hospital under the care of Dr. C. L. Dana.

He had had no previous illness; no history of either gonorrhea or syphilis. Had never suffered injury; never drank whisky; drank two glasses of beer daily. His one constant habit was tobacco chewing.

In the middle of April, 1912, he began to experience tingling pains "like needles" in both legs below the knees. These persisted, and to them were quickly added sharp cramp-like pains in the calves and in the backs of both thighs. He then began to suffer from numbness and weakness in the feet and ankles, with consequent

² Dr. Collins considered that the patient had a toxic affection of the cauda equina, due to some general condition.

difficulty in walking. He would frequently trip over small obstacles in his path, a circumstance explained by the rapid onset of double drop-foot. For two weeks before admission he had occasional incontinence of urine and feces. No symptoms were referable to the upper extremities nor to any of the cranial nerves.

Examination showed a thin, ill-looking man, appearing older than the age stated. Arcus senilis was present in both eyes.

Cranial nerves and upper extremities were normal.

Abdominal reflexes were depressed, but equal, on the two sides. Cremasteric reflexes were absent on both sides. Knee-jerks were present and equally depressed; ankle-jerks were absent. Plantars: sometimes of flexor, sometimes of extensor type. No ankle-clonus. Some wasting of all the muscles of the lower extremities, but marked atrophy of the anterior tibial muscles on either side. Bilateral foot-drop. No anesthesia or analgesia; temperature sense normal. No diminution in deep muscle pain sense; complete loss of postural sense in the toes of both feet.

The urine showed a faint trace of albumin; no sugar; a few hyaline casts.

The cerebrospinal fluid was clear and showed two lymphocytes to the cubic mm.; no tubercle bacilli; Noguchi and Wassermann tests were negative. The Wassermann test in the blood-serum was also negative. The blood-picture was that of a mild secondary anemia, with a hemoglobin percentage of 74. Considerable pyorrhea alveolaris, than which no other septic focus could be found.

From the date of his admission this patient's condition grew steadily worse. Paralysis was progressive, so that on July 26 there was marked weakness in the thigh muscles, this being more evident on the right than on the left side. Wasting had become so marked that it was difficult to say whether or not it was localized, and of segmental or root type.

The abdominal reflexes were present, but weak in all four quadrants. Cremasteric reflexes were absent; knee- and ankle-jerks were absent. Plantar reflexes bilaterally were of extensor type.

All forms of sensibility were then found to be lost in the second, third, fourth, and fifth sacral root areas of both sides, and markedly diminished on the right side in the third, fourth, and fifth lumbar and on the left side in the fourth and fifth lumbar root areas alone. (Fig. 6.) Postural sense; five errors in five trials in the toes of both feet.

Sphincter reflexes; bladder, complete retention; rectum, complete incontinence.

On July 29 Dr. Hartwell operated. The laminae and spinous processes of the ninth dorsal to the fourth lumbar vertebrae were removed. A careful search failed to reveal any tumor growth, but the conus and the caudal roots were seen to be much swollen and of a deep red color.

The patient failed to rally adequately after the operation; the lungs became edematous, and on August 12 he died.

Permission was granted to enlarge the wound made by operation. This was done by Dr. Hall, who succeeded in removing the major part of the cord, with its roots; the sacrum and its foramina were found to be macroscopically normal. Weigert-Pal sections showed inadequately an ascending degeneration, especially in the posterior columns. This degeneration steadily decreased as one went upward.

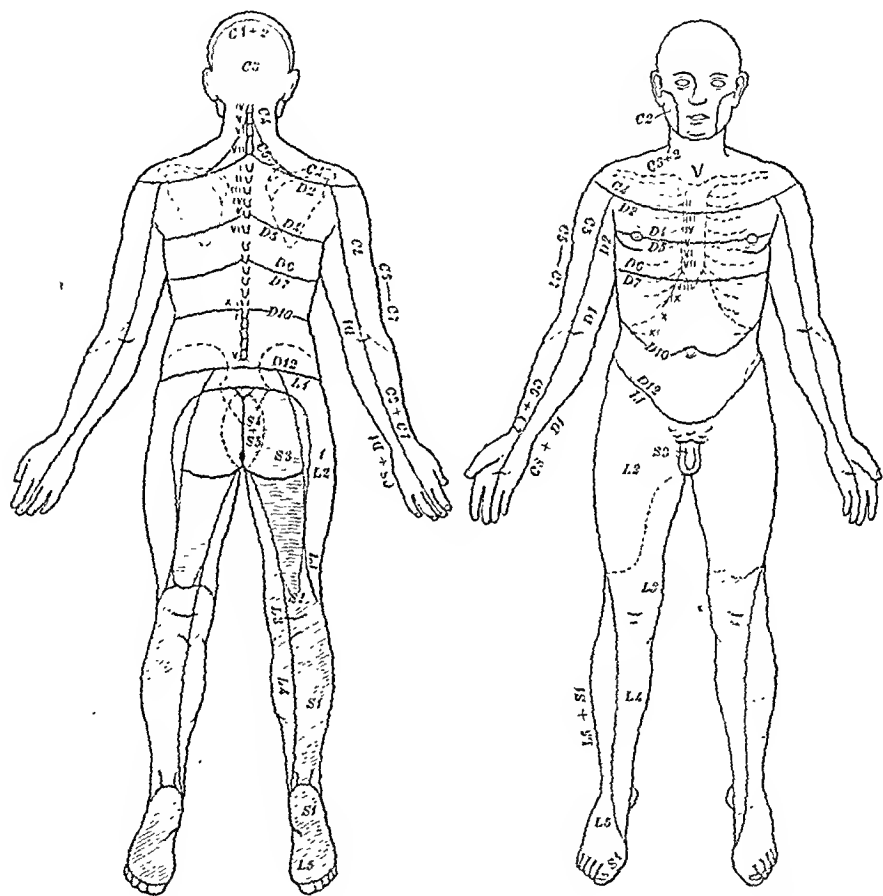


FIG. 6.—CASE V. F. K. Transverse shading, complete loss of all sensation; oblique lines, marked diminution.

ANALYSIS OF SIGNS AND SYMPTOMS. The histories of these five patients, while they are spread over various periods of time, are almost exactly alike in the nature and sequence of incident. In the third and fourth patients the symptoms were progressive in each for about two years, in the second for about one year, and in the first for but six months.

Pain was present in all from the beginning; it was sharp, shooting, and burning in character, and was felt almost entirely in the backs

of the thighs and in the calves. By the last patient it was described also as needling and cramp-like. In the first four patients the pain was, at the beginning, strictly unilateral, being felt in both legs after the lapse of some weeks or months. The leg first involved remained throughout the illness more affected than its fellow. All but the third patient complained much of tingling and numbness, involving sometimes the feet, sometimes the knees, and in the last two patients the entire surface of the lower extremities.

Atrophy of the anterior tibial muscles, with loss of the power of dorsiflexion at the ankle, was a prominent feature in four of the series; in the exception (Case III) there was a spasticity of the lower extremities, which was more marked on the right than on the left side. This was an important deviation from the symptom-complex, as we have become accustomed to recognize it, but the characteristic pains, the sensory changes, and the lesion of the caudal roots, identical with those of the other patients, furnish just evidence for the alignment of this patient in our series.

The objective sensory changes showed an astonishing uniformity; in all, the main incidence of the disease had fallen on the lowest roots of the cauda, the sacral roots were always affected, and with the utmost severity. In one patient (Case III) all the lumbar roots were also involved though to a somewhat lesser degree than were their more lowly placed fellows. In three only had the lowest lumbar roots become diseased to such an extent as to abolish or depress function.

As would be expected, the more markedly the lower sacral roots were involved the more complete was the sphincter disturbance. The disorganization of the functions of the bladder and rectum was complete in all but the third case, in which preeipitaneity and frequency of micturition prevailed. In that case, however, the destruction of function of the roots as gauged by the morbid sensory findings, while more diffuse than in any of the others, was considerably less complete.

The first, third, and last cases showed that disease had produced destructive changes in the cord itself; in them the plantar reflex was of the pathological extensor type.

The abdominal reflexes were present in all of the patients. In but one were the ankle-jerks obtained in the affected limbs. The knee-jerks became lost, as in the last case, coincident with the upward progress of the disease.

None of the patients gave either a history or indication of luetic infection. In all, the Wassermann test was carried out in both the blood and cerebrospinal fluid, with completely negative results in every instance.

In only one case did the cerebrospinal fluid give any indication of the presence of a disease condition within the dura, and in it (Case II) it was of doubtful interpretation, showing a negative

Wassermann test and an increased amount of globulin, with twenty lymphocytes per cubic centimeter, a cytological count, insufficient to accompany any tuberculous process.

ANATOMICAL FINDINGS. The conditions found at operation were the following: In two patients a large number of the caudal roots and in the other three all the roots were swollen, congested, and of a bluish-red color (Fig. 7). The difference between the color of these nerves and the color of the normal nerve roots was striking and easily recognizable. The changes seemed to be due to an intense hyperemia on the surface of the nerves, and extended into the nerves themselves. In one patient (Case 4), in whom a piece of posterior root was excised for histological examination, the entire nerve on cross-section looked discolored. Fine bloodvessels hardly visible to the naked eye could sometimes be traced upward on the nerve roots to the conus, where they formed a fine net-work in the pia mater.

Adhesions between the nerve roots were present in only one case; in the others the only changes were swelling and discoloration.

In all five patients the inner surface of the dura was smooth and glistening, and without signs of inflammatory change though in two of them a few small areas of hyperemia were observed. No gross change was observed in the conus or lumbosacral cord.

The cerebrospinal fluid was normal in appearance in four patients, while in one the color was more yellow than is usual. The amount of fluid which escaped when the dura was incised was considerable in several of the cases, but was no more than one often finds within the dural sac.

PATHOLOGICAL REPORT. CASE IV.—Percy M. A small fragment, $1\frac{1}{2}$ by 7 mm., of one of the posterior sacral roots was received in formalin. Preparations were made after Marchi's method and the Mann-Alzheimer and Mallory-Jacobson methods. In the Marchi preparations a low grade myelin sheath degeneration was present, involving approximately one in twelve or fifteen of the nerve fibers. With the Mann-Alzheimer stain relatively the same proportion of nerve fibers appeared to be affected, the axis-cylinders showing various degrees of swelling, loss of normal staining reaction, some of them showing granular degeneration, fragmentation, and absorption.

The danger of mechanical injury in the manipulations necessary for removal of the nerve root which might produce certain artifacts, resembling a true Marchi reaction, probably can be excluded, and though the material was limited in amount, the preparations appeared fully convincing for the changes described.

CASE V.—F. K. The spinal cord was received in formalin. There was some distortion in fixation of the lumbosacral cord, and identification of nerve roots and segments was uncertain. The external appearance of the cord was not remarkable, except that the dura

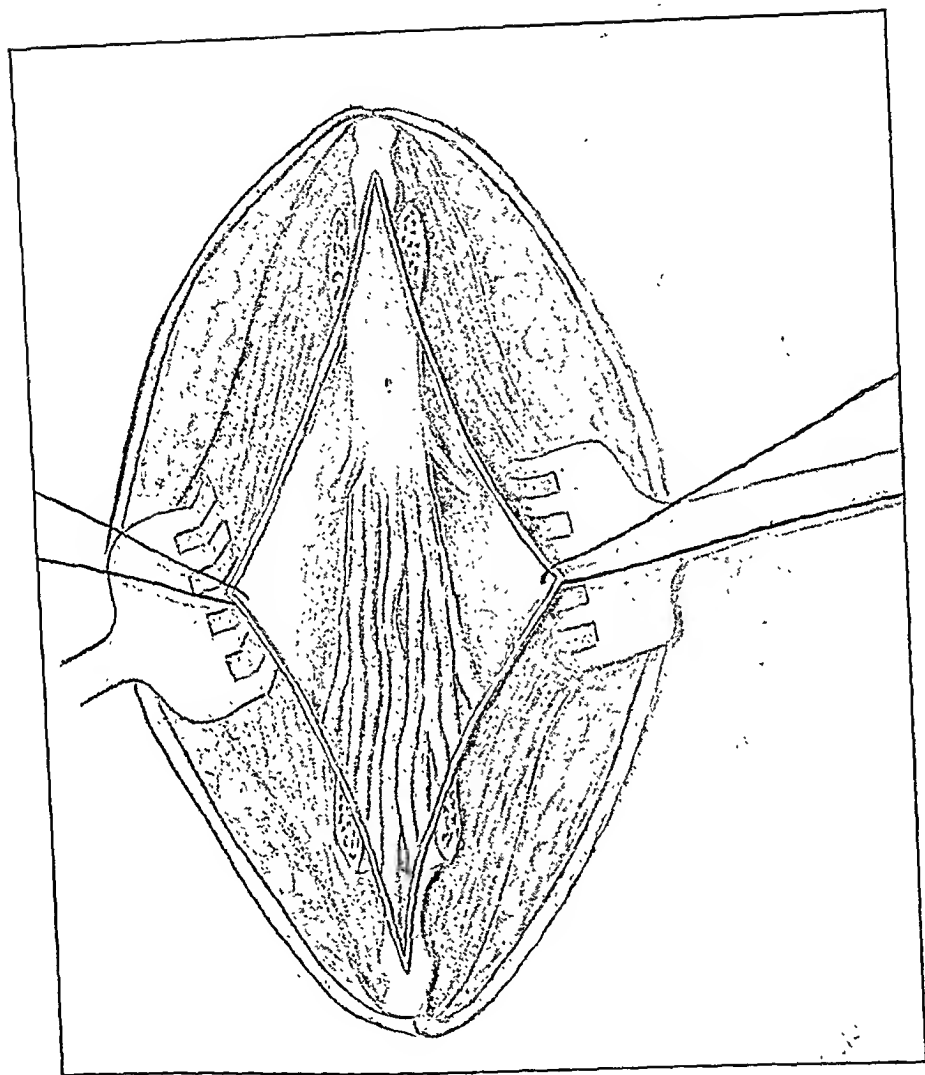


Fig. 7.—Case II. Mrs. St. J. Characteristic Swelling and Discoloration of the Nerves of the Cauda Equina

covering the cauda equina was congested, and on cross-section appeared moderately thickened.

The dorsal roots of the cauda equina were considerably injected, the central as well as peripheral vessels of the individual nerve roots standing out as black points. There were light adhesions between the posterior sacral roots, due apparently to an increase of the intervening tissue. Only portions of the lumbosacral root ganglia were present. The vessels of a number of these roots were considerably engorged; one of them contained a blood-clot about 6 mm. in diameter in the centre of the nerve root, just proximal to the ganglion.



FIG. 8.—Mann-Alzheimer axis-cylinder stain of a posterior sacral nerve root. Showing (a) swelling, (b) degeneration, and (c) absorption of the axis-cylinders as observed in cases F. K. and Percy M.

On transverse section of the cord the marginal afferent tracts appeared rather translucent. Slices were taken from the cervical, thoracic, and lumbosacral regions of the cord and from the cauda equina for alcohol embedding, for Weigert and for Marchi studies; other slices from the same regions were placed in a fluochrome-copper acetate mixture for neuroglia and axis-cylinder stains, and frozen sections were prepared with Herxheimer's Sharlach R stain and Spielmeyer's myelin sheath stain.

A summary of the microscopic findings follows: The meninges

of the cord at all levels were free from any lymphoid or plasma-cell infiltrate, and there was no evidence of syphilitic meningitis or endarteritis found at any level of the cord. In the dura covering the cauda there was some evidence of external chronic pachymeningitis and also internal serous hemorrhagic pachymeningitis, with a thin false membrane formation between the dura and pia-arachnoid. The larger spinal arteries, for example, the anterior spinal, showed a low-grade athero-arteriosclerosis. In the region of the cauda equina, however, there was a relatively high-grade arteriosclerosis involving not only the larger but the smaller arterioles



FIG. 9.—Hematoxylin and eosin preparation of one of the sacral root ganglia showing degeneration of ganglion cells, proliferation of the capsule cells, a number of which present amyloid forms, and passive or active neuronophagia.

supplying the individual nerve roots. The media and adventitia showed hyalin degeneration, the intima in its deeper portion showed similar changes; but toward the blood-stream were rather round clear cells, with vesicular nuclei, sometimes several cell layers thick. In a number of the smaller arteries and arterioles the lumina were very considerably reduced by this process. The central and marginal veins of the individual nerve roots were uniformly distended with blood; especially was this true for the posterior nerve roots of the cauda.

At the point where the dorsal roots penetrated the dura, chronic

inflammatory tissue elements, a few lymphoid cells, and fibroblasts were seen, but no plasma cells. The ganglion cells of the posterior roots of the cauda showed a variety of diffuse alterations, many of which might be regarded within the range of normal change, considering the age of the patient. A number of the cells, however, showed evidences of degeneration, indefinite irregular cell outlines with disappearance of the stainable substance, a marked increase in the amount of pigment, displacement of their nuclei, the membranes of which were often absent, and the nucleoli enlarged and vacuolar. About some of these cells the capsules were often several cells thick, and evidence of a passive or active neuronophagia was present.

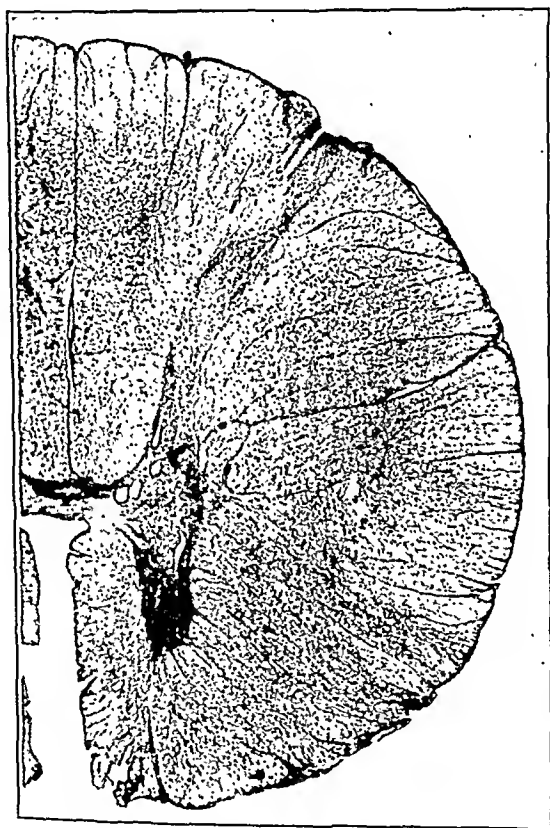


FIG. 10.—Mann-Alzheimer preparation of the thoracic cord, showing extensive degeneration of nerve fibers as well as much of the neuroglia in the ventral, lateral, and posterior columns of the cord.

A number of the posterior lumbosacral roots stained after the Mann-Alzheimer axis-cylinder methods showed a number of nerve fibers in different stages of degeneration, that is, swelling, vacuolization, granular degeneration, and absorption of the axis-cylinder as well as myelin sheath. Regenerative changes were not found with certainty. The axis-cylinder myelin-sheath degeneration appeared relatively recent, and evidences brought by the other

methods would seem to confirm this view. The total destruction of the posterior root fibers appeared limited and seemingly insufficient to explain all the root symptoms in the case.



FIG. 11.—Herxheimer Scharlach R fat-stain of the cervical end showing in addition to the degenerations equivalent to those observed in the thoracic region, the presence of granule cells in the areas undergoing degeneration.

Within the cord itself the intramedullary fibers of the sacral and lower lumbar cord segments were essentially free from myelin-sheath or axis-cylinder degeneration. In the midlumbar region and increasing in the thoracic and extending through the cervical segments there was a high-grade, complete degeneration of the nerve fibers composing the major afferent systems of the cord, namely, ventral spinocerebellar fibers, ventrolateral and dorsolateral spinocerebellar and spinothalamic fiber systems, and in the dorsal columns moderate degeneration in the dorsomedial as well as in the dorsolateral columns. The cord degenerations were essentially bilaterally symmetrical. Thus the degeneration involved both the posterior root fibers in their intramedullary course, but mainly the secondary afferent systems of the cord related to these were almost totally destroyed.

INTERPRETATION. A tuberculous or syphilitic meningomyelitis or neuritis can be definitely excluded, no lymphoid or plasma cell exudate or luetic type of endarteritis was present. In addition to the evidence of a chronic degenerative type of arteriosclerosis there was the intimal proliferation described above, which resembled or was identical with the reaction encountered in some of the acute infections or toxic processes, the intimal cells often appearing increased in number and the nuclei and cell bodies round and vesicular. The reaction is strongly suggestive of a relatively acute or subacute irritation, secondary rather than primary to the disease process.

The degeneration of the nerve fibers and cells in the posterior lumbosacral roots of the cauda equina appeared to be relatively recent in origin, days or weeks rather than months in duration, and compared to the cord involvement, minimal in severity and extent; the cord degeneration stands out distinctly as the most affected district. Whether the intraspinal fibers are more vulnerable than the peripheral root fibers or whether proportionately severer symptoms may arise from relatively slight injuries to the latter is perhaps a question.

The anatomical findings and to a degree the clinical in Case F. K., show a mixed condition, with a preponderant involvement of the afferent spinal fiber tracts.

In a complete and careful examination of the literature back to 1906, and in many authorities of an earlier date, we have not been able to find proved cases of the kind here described. Many are quoted which might be clinically relevant, but they are without confirmation by operation or autopsy. Before the era of luetic serology many of these were considered to have been syphilitic in nature, with, however, apparently often incomplete justification.³

One case, however, reported by Laiguel-Lavastine and Verliac,⁴ clinically identical with ours, was of undoubted specific origin. There only the right half of the cauda equina was diseased, in accordance with which the patient gave a history of pain in the sciatic distribution, weakness in the leg, drop-foot, loss of knee, ankle, and plantar reflexes, all on the right side, with retention of urine and loss of all sensation in the skin areas on the right side corresponding to the fifth lumbar and all the sacral roots.

The patient gave a history of luetic infection, and in addition to the signs already cited, had those corresponding to a previous cerebral thrombosis affecting the left side of the body. On autopsy there was found a meningoradiculitis of the right half of the cauda

³ Gierlich, *Deutsch. Zeit. f. Nervenheilkunde*, xviii, 322; Cassirer, *ibid.*, 1907, xxxiii, 401.

⁴ *Rev. Neur.*, Paris, 1908, xvi, 179-182.

equina, with marked matting together of the roots. This inflammatory process was looked upon as being of specific character, because of the hyalin degeneration and periphlebitis of certain posterior radicular veins. There was also present an ascending degeneration in the cord affecting almost entirely the posterior columns of the right side.

This one case is sufficient to show that changes in the caudal roots as a result of lues, and perhaps tuberculosis or leprosy as well, may produce a clinical picture necessitating a topographical diagnosis identical with that in our patients; but these cases of ours, on the other hand, show that apart from the outstanding systemic diseases, there may occur degeneration and loss of function in the caudal roots with, in advanced instances, ascending degeneration in the cord as well.

It might be argued that the five cases here reported are examples of a localized specific meningitis, but opposed to this contention is the absence of either a luetic infection or luetic serological findings, and the absence of distinct meningeal changes in any one of them. In several of our patients there was a history of trauma which preceded the beginning of the symptoms by many years. In none had the trauma been of recent date, and in none had a lumbar puncture been performed so recently that the congestion of the roots could have had any connection with that procedure. As we have already stated, the operation in our cases failed to reveal any lesion either within the dura or outside the membranes, or in the bony parts of the spine, excepting the peculiar swelling and discoloration of the nerves of the cauda equina.

It is of no little interest that this same caudal discoloration has been observed in one of the lower animals, the horse. In 1909 Marek⁵ published the report of a disease in a horse, with autopsy, which was in all respects similar to the disease in our patients. The animal began to have colic and to suffer from constipation. Later it developed marked weakness of the hind legs and retention of urine, with loss of sensation around the buttocks, in the anal region, and down the backs of both thighs. The patellar reflexes were depressed. The horse was killed, and at autopsy a marked congestion of the cauda equina and the surrounding pia mater was found. There was considerable connective tissue proliferation around the red and swollen lumbar and sacral nerve roots. A collection of blood external to the spinal column was evidently the result of an old trauma. Histologically the roots showed intense congestion and small round-cell infiltration, with disappearance of many of the nerve fibers. There was some ascending degeneration in the posterior columns of the lower dorsal and lumbosacral cord. Marek refers to similar cases reported by Marchand Alix and by Dexler,

in veterinary journals, but we have been unable to obtain these publications.

Marek describes the condition as a neuritis of the cauda equina.

The clinical condition in our patients seems to have been quite similar to that described in the horse, and the findings at operation were very like those found at the postmortem examination in the animals.

We have, therefore, been forced to the suggestion that our cases and perhaps some of those in the literature with like histories are examples of a true toxic neuritis of the caudal nerve roots. The probable existence in man of such a disease has been contended by several writers (Balint and Benedikt,⁶ L. R. Muller⁷ Raymond⁸), and has been produced experimentally by Orr and Rows⁹ who repeatedly have shown toxins to be capable of travelling from the sciatic and other nerves to the posterior root ganglia, along the spinal roots, and upward in the cord.

In their animals the signs of inflammatory reaction and of degeneration in the cord were inversely as the distance from the toxic focus, and were the result in each case of an infection of the lymphogenous paths.

It is our belief that our cases are examples of a morbid process akin to that produced experimentally by others, and it is our hope that in the future the study of other cases may make more plain the nature of the infection or toxemia and the possibility of its cure.

PRIMARY TISSUE LESIONS IN THE HEART PRODUCED BY SPIROCHETE PALLIDA.¹

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ALL recent statistics show a marked increase in the occurrence of cardiac disease, and various theories have been advanced to explain this increase. Alcoholism, nicotinism, nervous strain, overeating and drinking, intestinal intoxications, chronic infections, etc., have been given as the factors responsible for the myocardial affections that are seen with an apparently increasing frequency,

⁶ Deutsch. Zeit. f. Nervenheilkunde, xxx, 1.

⁷ Nouvelle Iconographie de la Salpêtrière, 1895.

⁸ Jour. Ment. Sci., London, 1910, lvi, 86-89; Rev. Neur. and Psych., 1912, x, 405-438.

⁹ Presented before the Section of General Pathology, International Congress of Medicine, London, August, 1913.

⁷ Ibid., xix and xxi.

but there is little unanimity of opinion as to the relative importance of these etiological agents. That syphilis plays an important role in the production of cardiac disease has long been suspected, and statements to this effect occur in the majority of text-books, usually unsupported by any pathological evidence. The truth of the matter is, that before the discovery of the *Spirochete pallida* as the etiological agent of syphilis, the pathologist himself recognized but few lesions of the heart as essentially pathognostic of syphilis. As to the significance of the gumma, he had no doubts; but gummas of the heart are relatively rare, hence his actual proof of cardiac syphilis became restricted to those instances in which the gumma was present. The frequent association of forms of chronic myocarditis, fibroid heart, anemic infarction of the myocardium and coronary sclerosis, with other pathological evidences of syphilis elsewhere in the body, such as tabes, parcsis, gumma of the brain or liver, aortic aneurysm, bone lesions, orchitis fibrosa, etc., has given the pathologist a strong leaning to the view that the heart is one of the most frequently affected organs in syphilis. In my own experience this has been the case, and I consider the most frequent pathognostic lesion-complex of syphilis to be that shown by the heart, aorta, and the orchitis fibrosa syphilitica of the testes. To these, a fourth lesion could be added as next in constancy of occurrence, the presence in the adrenals of small areas of plasma-cell infiltration.

That these lesions are actually syphilitic could only be assumed upon the strength of circumstantial evidence before the demonstration of the *Spirochete pallida* gave us a positive finding by which the diagnosis of syphilis could be made absolute. The whole pathology of syphilis must then be worked over from the standpoint of this new criterion, and this is particularly true of the affections of the heart long supposed to be syphilitic, but which from their nature could not be positively determined to be so. From this point of view I have been for several years engaged in a study of cardiac syphilis based upon the occurrence of the *Spirochete pallida* in the tissues of the heart, and the results of this study, insofar as the primary tissue lesions of the heart muscle are concerned, I wish to give here in a condensed form.

The material studied consists of two hundred hearts, fifty of congenital syphilis and one hundred and fifty of acquired syphilis. They represent all ages and all stages of the disease; the congenital cases are mostly newborn and young children, the acquired cases mostly adults in middle life with a history of old infection. The number of active secondary stage cases in the adult is small, but sufficient to trace the development of the lesions through successive stages. The Levaditi method in its original form has been used chiefly in this work, as it still remains the most satisfactory method for the demonstration of the spirochete in sections. For the study

of the tissue changes themselves the ordinary staining methods have been employed, with resort to special stains for special purposes, whenever this was considered necessary to determine the nature of the lesion. As a result of this study the primary lesions of cardiac syphilis may be described as follows:

PARENCHYMATOUS. *Localizations of Spirochetes in the Myocardium without Recognizable Tissue Lesions.* Large colonies of spirochetes may be found in the myocardium, either in the tissue spaces of certain muscle areas, or about the bloodvessels, without any changes in the neighboring heart muscle that can be recognized by any of the technical methods employed at the present time. The muscle stains as well as normal heart muscle; it contains no vacuoles or granules, and presents all the appearances of normal muscle. The spirochetes lie in the intermuscular spaces, often in great numbers. Sometimes they appear within the muscle substance, as shown in cross-sections, but this is not common. Such findings are most frequent in congenital syphilis, but such collections of spirochetes without recognizable myocardial changes are found also in acquired syphilis, particularly in active secondary stages or early tertiary.

Pale Degeneration of the Heart Muscle in Association with Spirochete Pallida. One of the earliest recognizable changes in the heart muscle in areas containing spirochetes is the loss of color in the muscle fiber and its failure to take eosin in the normal way. Compared with normal areas, such affected muscle appears light and clear, with a loss of its striations, and shows vacuolated or light-staining nuclei. In the severe grades of this change the muscle passes so insensibly into the connective tissue that it is difficult to separate the two, so closely do they come to resemble each other in ordinary stained sections. Vacuoles may or may not be present in these fibers. The appearance of the fiber is not wholly like that of Zenker's necrosis, as it is less waxy or hyaline, appearing "washed-out." The fibers are also smaller than normal. This form of degeneration may occur as a purely parenchymatous change, but is most commonly associated with interstitial changes, particularly with the mucoid edema so frequently seen in congenital cases. This change is probably to be interpreted as being of the nature of a serous atrophy or liquefaction necrosis, but there is never any fraying-out of the cell protoplasm as in ordinary liquefaction necrosis.

Fatty Degeneration. A marked fatty degeneration of the cardiac muscle is often the only tissue lesion associated with the presence of the spirochete colonies in the myocardium. It occurs as a focal change, visible to the naked eye as yellowish pin-head spots, but often larger. Microscopically, the fibers are atrophic and filled with large droplets of fat, the droplets, as a rule, being larger than those commonly seen in fatty degeneration of the heart

muscle in such conditions as anemia, phosphorus poisoning, etc. Usually two or three large vacuoles replace the cytoplasm. This fatty degeneration of the fibers occurs also in the muscle surrounding the areas of interstitial infiltration and proliferation. In these areas of fatty degeneration, fewer spirochetes are usually found than in the focal areas of fatty degeneration unaccompanied by interstitial changes. In the case of severe vascular and perivascular infiltration and proliferation, irregular areas of fatty degeneration occur along the affected areas, but this is probably a secondary change to the circulatory disturbance. In the focal areas without other changes than the mere presence of the spirochetes, the occurrence of the fatty change must be explained as due to the presence of the organism, the latter probably robbing the tissues of their oxygen and food supply. Following the focal fatty degeneration, there may occur later a deposit of lime salts, so that focal areas of calcification can be produced by syphilis, and their occurrence in the myocardium should lead to a suspicion of this infection.

Simple Atrophy. Colonies of spirochetes can sometimes be located by the presence of focal areas of simple atrophy, the muscle showing no other change than a marked reduction in size. The interstitial substance may or may not be increased or show proliferation, and the pale degeneration and fatty degeneration may be associated with the atrophy.

Necrosis. In virulent cases of congenital syphilis in which the tissues of the body show enormous numbers of spirochetes, yellowish or light-colored areas may be found in the myocardium as well as in other parts of the body. These areas rarely exceed 5 mm. in diameter, and are usually much smaller. In the heart the muscle in these areas appears as fine fibrillæ without nuclei, or is entirely absent, its place being taken by a collection of lymphocytes, plasma cells, and fibroblastic cells. Around the borders fibers showing transition stages of liquefaction necrosis are seen, and the surrounding tissue appears as in a chronic edema, the tissue elements being pushed apart and the spaces filled with a fine albuminous precipitate, a mucoid substance and cells. With the specific mucin dyes, as kresyl violet, reactions for mucin are almost always obtained in these areas of liquefaction necrosis. Such changes are absolutely independent of any vascular changes, and are wholly the result of the spirochetes that lie packed in great numbers in these necrotic areas.

INTERSTITIAL CHANGES. Edema. In syphilitic hearts, particularly in congenital syphilis, pale areas, moist and translucent, may be seen even with the naked eye, or the entire heart wall may be very pale, translucent, and moist. On microscopic examination the pale foci are found to be areas in which the changes are wholly suggestive of edema. The muscle fibers are pushed apart, the reticulum is fibrillated and contains fine granules, and the number of wandering

cells is more or less increased. The presence of fat vacuoles in the muscle fibers adds to the general picture of a severe local edema, so that the average observer would pass it as an edema. But the Levaditi preparations show these apparently edematous areas to be filled with spirochetes, and the mucin tests show frequently the presence of a mucin-like substance, so that the edema is more of the nature of a myxedema. In these areas the spirochetes often appear closely applied to the capillary walls. Some of these areas are relatively poor in cells, but the majority show a fibroblastic proliferation, large, pale, epithelioid cells occurring, their cell bodies lightly staining, and their whole appearance washed out. Mononuclear white cells, plasma cells, and lymphocytes are present in varying numbers; and every transition exists between these pale, non-cellular, watery areas and those containing many cells.

Interstitial Proliferation. This may occur as the first recognizable tissue lesion, but usually after it has reached a certain point the parenchyma shows degenerative changes also. In the heart the proliferation appears to be always primarily vascular or perivascular, the endothelial cells of the capillaries proliferating and forming rods and groups of pale epithelioid cells, the capillary becoming thicker and thicker as the mass of cells in its walls increases. Now capillaries are produced and the area may come to be highly vascularized, but the new vessels are quickly obliterated by the proliferation of the wall. In the larger vessels, particularly in the arterioles, the proliferation is almost wholly perivascular and the spirochetes are found in great numbers in the perivascular lymphatics. Later these areas may become fibroid, and every possible transition stage is found between the focal edemas, and the areas of proliferation that may be interpreted as non-caseating gummas when sharply localized. In the congenital syphilis cases caseation of these areas must be very rare, as we have never found it. Such areas of proliferation without caseation exist also in acquired syphilis.

Myxoma-like Areas. A striking finding in the hearts of congenital syphilis is the occurrence of round, translucent areas that microscopically suggest myxomas and have been mistaken for such. With ordinary stains, hematoxylin and eosin, they appear as sharply circumscribed, spherical areas in which the heart muscle fibers have practically disappeared, only a few atrophic fibrillæ being left. A gelatinous tissue containing branching epithelioid cells and lymphocytes forms the main part of the area and new capillaries occur in it. Mucin tests show the presence of a large amount of mucin, so that the resemblance to a myxoma is greater still in preparations stained in this manner. Levaditi preparations show the presence of spirochetes in varying numbers in these areas, although the number is usually not so great as in the focal fatty areas and edemas. It is probable that the infection is a less viru-

lent and more sharply localized one. These areas may be regarded as young or undifferentiated gummas, myxogumma, without fibroid change or caseation, the tissue remaining in a fibroblastic semigelatinous state. The infiltration of lymphocytes and plasma cells is often very slight, so that this adds to the deceptive appearance of this formation, and if the Levaditi method for the demonstration of spirochetes were not carried out, the true nature of the process would not be detected.

CONCLUSIONS. These studies of cardiac syphilis would show that the primary lesions produced by the *Spirochete pallida* may be either parenchymatous or interstitial. The parenchymatous lesions are a peculiar pale degeneration, fatty degeneration, simple atrophy and necrosis; the interstitial lesions are the occurrence of a peculiar form of edema (myxedema), vascular and perivascular infiltration, and localized myxoma-like formations. The parenchymatous changes may occur absolutely independently of the interstitial, and the latter may be found with no associated changes in the neighboring heart muscle. The more marked the interstitial changes the more likely are parenchymatous changes to be associated with them, but the most marked parenchymatous lesions may occur without any interstitial changes. The purely parenchymatous lesions are found especially in virulent congenital and active secondary and early tertiary syphilis; in milder and older infections the interstitial changes, particularly the localized vascular and perivascular proliferations, predominate. The myxoma-like formations resembling undifferentiated gummas also occur in more localized and milder infections.

It is also of great importance to know that the heart is so frequently the seat of spirochete localization. The cardiac localization of spirochetes we have found to be more common than the hepatic. Spirochetes may be found in great numbers in the heart when no others can be found elsewhere in the body. In such cases the cardiac muscle may also show no lesions that, according to the older knowledge, would be classed as syphilitic, indeed, no organ or tissue may show any histological signs of syphilis even when the organisms are present in great numbers. That syphilis can produce purely parenchymatous lesions primarily in the myocardium opens up greatly the possibilities of this infection as a factor in the increasing myocardial affections of unknown origin. To what extent the *Spirochete pallida* is the etiological agent in these conditions cannot be estimated with certainty at the present time, but my own experience would make me believe that syphilis, both congenital and acquired, is the most important etiological factor in the production of cardiac disease, both myocardial and endocardial.

THE MECHANISM OF PROSTATIC RETENTION.

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SEVERAL studies have recently been published on the mechanism of prostatic retention, concluding with the statement that prostatic hypertrophy is not the cause of prostatic retention. Their inference is that prostatic hypertrophy may exist without retention, and that the true cause of retention is to be sought rather in the bladder muscle or innervation than at the bladder neck. They further support this theory with many reported cases of what the French call "prostatism without a prostate." together with Albarrin's theory of muscular weakness.

Two clinical types of prostatic retention may be distinguished: chronic, incomplete or complete retention, and acute complete retention. Though they are related, it is better to discuss their mechanism separately, beginning with the former, the chronic type, since the elucidation of this makes the interpretation of acute retention a matter of but a few words.

CHRONIC PROSTATIC RETENTION. Prostatic retention represents the interaction of two forces, the bladder muscle and the obstruction. The importance of each of these is best understood if they are discussed separately.

THE BLADDER MUSCLE. In discussing the action of the bladder muscle it is convenient to include the nervous mechanism that instigates the act of urination. We have, therefore, to note:

The condition of the muscle itself.

The condition of the nervous system.

The condition of the will.

The Muscle Itself. Suprapubic cystotomy on an old prostatic often reveals a bladder muscle that grossly resembles blotting-paper, and obviously possesses but little contractile force. Quite as often, however, one encounters a muscle with all the macroscopic and microscopic evidence of vitality. After prostatectomy upon these patients we find that the good or bad condition of the bladder muscle has little effect upon the ultimate result. The patient with the "blotting-paper" bladder is almost, if not quite, as likely to regain the power of emptying his bladder as the patient with the normal muscle.

I can recall many instances of complete cure after prostatectomy in spite of a "blotting-paper" bladder; nevertheless, these are a little more liable to incomplete relief by prostatectomy than are their brethren with more normal muscle.

For, supposing for the moment that obstruction at the bladder neck is an element of prostatic retention, it is evident that just

as a strong bladder may fight for a much longer time against an obstruction before it gives away; so, when the obstacle is removed, it must be more completely done away with to give entire relief to a sclerotic bladder than to a normal bladder.

Indeed, an experienced urologist can prophesy with a certain degree of accuracy that the patient with slight infection, and less than 100 c.c. retention, but undue urinary irritation and frequency, is likely to remain in this condition for a considerable time; while the patient who first comes to a physician after his bladder has silently reached chronic, complete retention with overflow will do badly. This prophecy is based in part upon differences in the tone of the bladder muscle. Furthermore, the progressive weakening of the bladder muscle doubtless is the main agency in the rapidity or slowness with which a patient passes through the first and second to the third stage of prostatic retention. Though here, again, the muscle is not the only element in the case.

The Nervous System. When the muscle of the bladder is seriously or completely paralyzed, as in tabes, the resulting retention is probably not solely due to weakness of the bladder muscle, for I have, by means of the Chetwood operation, satisfied myself that a diminution of the sphincteric obstacle at the bladder neck may result in considerable improvement in the symptoms of such patients.

As a striking example of this, let me cite the case of a patient, aged thirty-four years, operated upon in October, 1907, at which time he had been suffering from difficulty in urination for eight years, and for six weeks had been urinating every two hours, with incontinence both by day and by night. He showed a fairly constant residual urine of two ounces, denied syphilis, but had no patellar reflexes; his eyes reacted poorly, his prostate was normal, and he was sexually impotent. He had for a number of years suffered from lightning pains and paresthesia.

His convalescence after Chetwood operation was stormy on account of fulgurating pains, but he healed promptly. The fistula, however, reopened after two weeks, and did not close until December, 1907. Ataxia, which was not present before operation, gradually came on during the ensuing year, and now, six years after the operation, he is markedly ataxic, and speaks of himself as a broken man. Nevertheless, his urinary organs have given him absolutely no further discomfort. He urinates four times by day, not at all by night, and has no pain whatever with micturition.

A second tabetic, who had been ataxic for eight years, and used the catheter for seven: the residual urine varied from 100 c.c. to 500 c.c., and occasionally he had acute complete retention. The Chetwood operation revealed and divided a dense contracture.

His convalescence was also complicated by severe lightning pains. After operation he had complete retention for two weeks, and thereafter he learned that by holding his urine until the bladder contained at least 500 c.c. he could empty it down to 25 or 50 c.c. He continued in this condition until his death from pneumonia about eighteen months later.

This inability to urinate until the bladder is full I have found in a number of tabetics.

A third case, in acute complete retention, was unimproved in spite of two Chetwood operations by me, and several punch operations upon the bladder neck. A similar failure resulted from the cauterization of the neck of a paralysis following operation upon spina bifida.

The diversity of these results is due to the fact that a paralyzed bladder goes into a state of retention when there is even the slightest obstacle to urination at the bladder neck. Indeed, it is the paralyzed bladder that shows that curious combination of incontinence and retention not completely accounted for either by any large residual urine or a contracted bladder. In attempting the removal of this slight urethral obstacle to the emptying of the bladder, one is moved to great conservatism by the fear lest too bold an operation leave the patient more incontinent than before, and one is thus liable to remove only part of the obstruction in these cases where complete removal of the obstruction is most indicated.

The Will. The influence of the will upon retention of urine in typhoid and other wasting diseases was beautifully described by Dr. Samuel Alexander at the first session of the International Urological Congress. He ascribed retention in such cases to actual muscular weakness combined with weakness of the powers of attention. In some old prostatics I seem to have noted a similar unwillingness to take the trouble to empty the bladder. Quite recently an ancient Hebrew came into my service at Bellevue Hospital acutely overdistended, was relieved by suprapubic drainage, followed by prostatectomy under spinal anesthesia. His suprapubic wound healed within three weeks thereafter. Yet, to my great surprise, as soon as the fistula had healed he proved to have retention of urine, averaging about twenty ounces. The lowest amount we ever obtained was six ounces, the highest, forty-eight ounces. Yet his general condition remained excellent for the two or three weeks he remained in the hospital, and his family, who had apparently turned him over to us with high hopes that they might get his savings bank account, rather despaired of my ability to kill him, and so refused permission for any further operation. It is my impression that had the old man been moved by a real desire to empty his bladder he probably could have done so. Doubtless others have seen similar cases,

or at least they have seen that type of case in which after prostatectomy the patient habitually retains from two to four ounces of urine. If you inject into the bladder even a mild solution of potassium permanganate, or silver nitrate, this is emptied out to the last drop.

It seems fair, therefore, to state that the strength of the bladder muscle plays a large part in certain cases of prostatic retention; and that if muscular weakness is the predominant cause of retention, removal of the obstacle at the bladder neck, which is the occasion of the retention, is a more delicate matter than when the bladder muscle has retained its strength.

THE ENLARGED PROSTATE. Let us repeat once more, with Sir Henry Thompson and his followers, that not more than half of the men whose prostates are enlarged suffer from prostatic retention, and let us add that some of those who suffer from prostatic retention have no hypertrophy of the prostate. These are the two facts which, as we said in the first place, impress those who deny that enlargement of the prostate has anything to do with retention of urine. If they will modify their claim and state that the size of the prostate has no bearing upon the amount of residual urine, we agree with them most heartily, but beyond this we cannot go. It is quite obvious that in most instances prostatic retention is due to hypertrophy of the prostate, and it is equally obvious that in most instances the removal by prostatectomy of the hypertrophied portions of the prostate relieves the prostatic retention. But in certain instances this is not the case. There are those who have no prostatic hypertrophy, and to whom, therefore, prostatectomy is not applicable, there are those upon whom prostatectomy has been done without any influence upon their retention of urine, and (let us not forget) there are not a few upon whom a Bottini operation or a shockingly incomplete prostatectomy results in a cure.

These cases require explanation, and lead us to investigate more particularly the changes at the bladder neck associated with the various pathological conditions that excite prostatic retention. Before passing to these, let us state, briefly and categorically, our views as to the role of prostatic hypertrophy in prostatic retention:

1. The mere fact of hypertrophy of the prostate is not of itself sufficient cause for prostatic retention.

2. In order to cause prostatic retention, prostatic hypertrophy must interfere with the outflow of urine from the bladder.

3. This interference may be due to deformity of the bladder neck (of which we shall speak in a moment) or to an actual compression of the urethra within the hypertrophied gland.

4. That this compression, or stricturing, of the urethra cannot usually be an important factor, is evident from several points of

view: In the first place, the urethra is not strictured but rather dilated, as a rule. In the second place, there is usually no obstruction whatever to the passage of a catheter through the prostatic urethra from the time it leaves the membranous urethra to the time it reaches the bladder neck. A canal that transmits an instrument so readily would scarcely offer any resistance to the passage of urine, however weak the bladder.

5. Hence, we are forced to the conclusion that even the lateral compression of greatly enlarged lateral prostatic lobes, probably has little or no effect in interfering with the outflow of urine.

We might note the fact that the occasional success of the Bottini operation in relieving retention due to considerable prostatic hypertrophy is evidence confirmatory of this opinion. We pass, therefore, to consider the nature of the obstacle at the bladder neck.

THE BLADDER NECK. In order to simplify the somewhat complex problem presented by the obstacle of urination at the bladder neck in a case of prostatic retention, let us at the outset exclude from consideration such unusual conditions as hypertrophy of the anterior lobe, or enormous hypertrophy of the middle lobe, or other eccentric growths, since these produce a mechanical obstacle rather different in its nature from that which we usually encounter.

We therefore confine our observations to the usual types of obstruction, which may be classified under the following heads:

1. Middle lobe hypertrophy, more or less pedunculated.
2. Lateral lobe hypertrophy, without a clinically recognizable middle lobe.
3. General hypertrophy, in which neither lateral or middle lobe are prominent.
4. General hypertrophy, in which middle or lateral lobes, or both, are prominent.
5. Contracted bladder neck.

It would obviously be quite impracticable, and happily it seems quite unnecessary, to consider the mechanical obstacle to urination, caused by these different pathological conditions *seriatim*. The obstacle is much the same whatever the cause. In order to appreciate its nature let us first compare the observations made by the examining finger when introduced through the perineum into the prostatic urethra of the normal case and the case in prostatic retention. Let us suppose, in the first place, a patient with stricture of the bulbous urethra that has been divided by perineal section. The finger is introduced into this wound, passes through the membranous urethra, usually tearing this somewhat, thence into the prostatic urethra, which is identified as a somewhat dilated portion of the canal that readily admits the finger, and thence into the normal bladder neck, recognizable as an elastic muscular ring, beyond which the tip of the finger may be pushed into the emptiness of the bladder cavity.

Palpation of this muscular ring reveals that it is not prominent upon the roof of the urethra, while it grows more prominent as it approaches the floor. Thus the finger lying in the urethra with its tip against the bladder neck pushes against that part of the ring which even in the normal state rises up to make a slight muscular bar between the floor of the urethra and the floor of the bladder. In prostatic retention this obstruction to the entrance of the finger into the bladder is much more marked. As the finger passes through the prostatic urethra it may encounter and note the presence of prostatic lobes projecting into the canal laterally, or from below, and at the bladder neck, but it also recognizes that the chief obstacle is at the neck of the bladder whether this obstacle be due to prostatic hypertrophy in the form of a middle lobe, or bar, or to sclerosis, in the form of a contracted bladder neck. Indeed, it recognizes that when the bladder neck is tightly contracted, this contraction occurs almost entirely at the expense of the floor, while if only the lateral lobes of the prostate are enlarged the obstacle to the entrance of the finger into the bladder is a veil or bar of bladder neck lifted up between these lateral lobes.

The same observation may be made if these various pathological conditions are examined from a suprapubic opening into the bladder. Whether there be a general "horse-collar" hypertrophy, a contracture, a lateral hypertrophy, or a middle lobe, the finger introduced into the posterior urethra recognizes that between it and the bladder, on the floor of the urethra, there is elevated an abnormal obstruction. This obstruction is the mechanical cause of prostatic retention. It arises from the floor and not from the roof, even in cases of contracture and of lateral prostatic hypertrophy, because the roof of the urethra is more fixed (by the pubo-prostatic ligaments) than is the floor.

The precise way in which this obstacle interferes with the outflow of urine from the bladder has never been absolutely proved. Unquestionably, it prevents the normal opening of the internal sphincter, thus causing the difficulty in starting the urinary stream. But why does it in so many cases reduce the bladder to a condition of partial retention in which the amount of residual urine is practically constant whether the patient stands upon his head or upon his feet? The explanation of the phenomenon is suggested by the fact that if a bubble of air is injected into the normal bladder this always issues after the last drop of urine is passed. In other words, the bubble floating on top of the urine under the vault of the bladder is the last thing to issue from the bladder in a normal urinary act. Moreover, if the bladder contains thick, tenacious pus delivered from a pyonephrosis, and lying upon its base, this pus will issue at the end of the urinary stream, and immediately ahead of the bubble of air which closes the stream.

If there is retention of urine neither the pus at the bottom of the bladder nor the air at its vault are extruded.

To explain these phenomena we must assume that as the bladder empties itself the trigone is somewhat elevated, forming the flare of the funnel, which in a normal bladder begins in the prostatic urethra, and the remainder of the bladder closes down upon this funnel, the lowest and highest points in the bladder cavity lying posterior to the trigone and being emptied last. But when there is retention the funnel is an inadequate one, the bladder neck fails to open as it should, and the result of the effort to squeeze out the last drops of urine is to close the bladder neck. The closure should be interpreted not as a sphincteric gripping, but as the driving of the prominent lower lip of the bladder neck against the upper wall of the prostatic urethra. If the closure were sphincteric a hard push might force it and drive out a few drops more of urine, but inasmuch as it is rather the application in the form of a valve of the prominent lower portion of the sphincter against its upper portion, the harder the patient strains the tighter does the valve close. The only way he can pass any more urine is by relaxing his muscles and permitting the sphincter to open a little. Then another effort may bring forth quite a flow of urine before the valve flaps shut again.

ACUTE COMPLETE RETENTION. Chronic retention is due fundamentally to an inability of the bladder sphincter to open until the bladder is partially full. Acute complete retention is due to a congestion and spasm at the bladder neck of such intensity as to apply the posterior lip of the sphincter against the anterior even when the bladder is full. Operation upon such a case does not reveal an impassible closure of the neck of the bladder, as would be the case were the obstacle a sphincteric or stricture-like one, and not a valve-like one.

The mechanism of acute complete retention, is, of course, the same in prostatic abscess as in prostatic hypertrophy.

One readily understands without further comment how various combinations of obstruction, congestion and spasm produce the many variations in the clinical phenomena of prostatic retention, while the gradual progress of the increase in the amount of retention of the urine as the months go by is due largely to gradual decrease in the strength of the bladder muscle.

PRACTICAL DEDUCTIONS. Several practical conclusions may be drawn from the above remarks. In the first place, since mere prostatic hypertrophy is not enough to cause prostatic retention, prostatic retention may sometimes be relieved by removal of the obstacle at the bladder neck without any attention to the prostate, even when this is hypertrophied. This the Bottini operation used to do blindly, and, as it were, accidentally, while the Chetwood

operation achieves it intentionally. I have several times relieved the retention, great or small, of a patient whose prostate showed bilateral enlargement, simply by dividing with the Chetwood instrument the bar at the neck of the bladder, while paying no attention to the enlarged lateral lobes. The same thing can sometimes be done when the median lobe of the prostate is hypertrophied, when it is in the form of a bar or a pedunculated lobe, though it is obviously safer under these circumstances to remove the bar or lobe. But the point illustrated by the success of the Chetwood operation is that an attack directed solely upon the bladder neck at its lowermost part can relieve prostatic retention. Yet when the prostate is considerably enlarged it were obviously futile to satisfy one's self with division or excision of the bar or middle lobe, for then the lateral masses at the bladder neck crowd in and still interfere materially with the opening of this orifice. Indeed, whatever the condition of the bladder muscle at the time of operation we can count upon this growing weaker as the years elapse. Hence our ambition should be to remove all possible obstacles to urination, including all hypertrophied portions of the gland.

But it cannot be too often repeated, the prostatectomy, the removal of the hypertrophied portions of the prostate gland must be looked upon only as a means to an end, that end being the removal of the obstacle at the bladder neck. Hence the technical disadvantage of perineal prostatectomy, especially for the neophyte who is likely to be satisfied with removal of the more immediately presenting portions of the hypertrophied prostate, while totally disregarding the obstructing bladder neck that lies beyond. Hence, also, the mechanical superiority of suprapubic prostatectomy, since the attack from above inevitably at least tears open the neck of the bladder, while this is the last region reached from below.

It has been our experience that no operation for prostatic hypertrophy will give 100 per cent. of cures among the survivors, for the peculiarities of healing after operation and the weakness of the bladder muscle may well frustrate our most intelligent efforts. Yet, in conclusion, we should like to insist in theory as we always have in practice that the problem of prostatic retention is a mechanical problem; that the bladder neck, and especially the elevation of its inferior lip, is the important mechanical obstruction, and that prostatectomy, suprapubic or perineal, total, subtotal, or partial, should be performed with the object of obliterating this obstacle at the bladder neck.

HYPERTENSION: A REPORT OF CASES UNDER PROLONGED OBSERVATION, AND A PROTEST AGAINST SOME IDEAS.

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HYPERTENSION is such a significant condition, that anyone who studies many cases should perhaps be permitted to express his personal impressions and experiences. Though it is not many years since much attention has been given to it, in the course of routine physical examination, it is surprising at present to see how frequently one meets intelligent patients, who have some information about the annoying condition. Frequently they presume to understand its significance and it alarms them, perhaps unnecessarily.

Before entering into any discussion of the subject, I wish to report some cases:

CASE I.—A patient, now aged fifty-four years, has been under close observation for the past seven years. He is the father of three healthy children. His previous history and habits are excellent. He is a prosperous manufacturer, and his business of recent years has simply driven him incessantly. When first seen he was complaining only of constipation, insomnia, a feeling of nervousness, restlessness, and pain in the calves of his legs, which annoyed him most at night or when away from his office. He loved good food and always had it. When first seen the physical examination was almost negative; abdominal and thoracic organs and nervous system normal also. Though he had a marked gastric hyperacidity, rather firm and full arteries, and a blood-pressure of 200. During these years of observation his systolic blood-pressure in the arm has varied from 160 to 230. Some of the latest observations of the tension, as established both by palpation and auscultation, showed a systolic pressure of 215 in the arm and 265 in the leg. There was possibly the same difference in the diastolic pressure, inasmuch as the carotids seemed to empty more completely during the diastole than did the femoral.

While this patient's urine is usually normal, it has often contained a trace of albumin and some casts. Bile and indican are frequently found. His liver is sore occasionally and slightly enlarged. And at those times one may find fault with the heart, either dilatation or hypertrophy with dilatation.

Now, in spite of any skepticism which physicians and post-mortem pathologists might have concerning diagnosis, I believe the patient has a beginning interstitial nephritis; some sclerosis

of the arteries, but so far little hypertrophy of the heart. The patient has always been rather apprehensive and introspective and worried about his blood-pressure and expectation of life. Though he has but few symptoms at present, he is much disappointed on account of inability to buy life insurance. To be restricted in diet and greatly deprived of meat becomes irksome to him. But a seven year's course of treatment has made its impression upon both patient and physician.

Moderate doses of nitroglycerin or any vasodilators cause violent headaches, and do not reduce the blood-pressure. Frequent hot baths followed by a slight sweat between blankets are effectual for comfort, though the pressure remains up. The occasional Turkish bath has the same influence. Treatment with the high-frequency electric current has been used faithfully without any reduction in blood-pressure. A few years ago the patient was kept in bed four weeks, and confined to his home several weeks longer, mainly to insure rest and isolation from the annoyance of a labor strike by hundreds of workmen in his firm's employ. At the same time he was having a strict diet and some medical treatment as well as hydrotherapy. This treatment made him feel better, but did not have any marked effect upon the blood-pressure.

His main line of treatment has been for the relief of constipation, by some exercise, suitable food, and much water. He had used cholagogues almost continuously. When deprived of these he does not feel well. Effectual medicines have been calomel, rhubarb, soda, magnesia, and Carlsbad powder; and when small doses of bromides are used, the effect is still more pleasant. Iodides have been taken faithfully at frequent periods for months, but with questionable advantages. While using salicylates and urotropin the urine usually contains less bile and indican, and the patient feels more comfortable. While this patient's blood-pressure has not been influenced much in seven years, he is, after all, comparatively free from symptoms when he pays constant attention to elimination. And in spite of a high pressure, which ought to concern anyone, he has been active in business. He cannot learn to be lazy, and now the question arises whether further attempt should be made to lower the pressure.

CASE II.—This case was first seen in 1906. The patient appeared at my office with a quart of whisky under his arm and a pipe in his mouth. He was aged eighty years, and sought relief from a slight skin affection and a stiff knee. He was never sick in bed. The physical examination was negative, except for arteriosclerosis, hypertension, and bile and indican in the urine. In April, 1911, he had an attack of pyelocystitis after his return to the city from New York, where he usually spent the winter, and where he also used more stimulants than elsewhere on account of his dislike for the water-supply of New York. He has abstained entirely

from the use of whisky ever since this attack of cystitis, though it was somewhat of a hardship at first, having been accustomed to take one or two quarts of whisky and sometimes more each week for the past forty years. When asked when he first began to use liquor, he said (with a clear mind) that he supposed about the time he could hold a bottle to his mouth. In May, 1912, he had a mild apoplexy and a partial paralysis of the right side. While the blood-pressure was over 200, it fell to 130 at the end of four weeks, with rest in bed, but returned to the former point soon after he began to move about again. While in bed he was treated with cathartics, hot packs, bromides, and small doses of iodides and nitroglycerin. As the nitroglycerin in more than one-drop doses every hour caused much headache, he refused the medicine. The iodides received the same condemnation. Now, in spite of prolonged alcoholism, arteriosclerosis, paralysis, and hypertension, there is no marked heart or kidney lesion. And one might wonder whether such a patient might not live indefinitely if he had begun to use iodides and various forms of buttermilk at about the age of forty to prevent high blood-pressure. It must be stated that the patient, now eighty-seven years old, has always lived in comfortable circumstances, provided by his own industry. He is not rich, but far from poor. He does not worry. When eating, he is abstemious and deliberate. His wife once told me that "Henry was never known to be in a hurry."

CASE III.—A man, now aged fifty-eight years, has been under observation for five years. He has been active and successful in business. Never idle a minute. He abstained from alcohol and tobacco, and excepting an attack of cholecystitis, he was never sick. He complained of constipation, dyspnea, insomnia, "lame all over." He had firm arteries, a blood-pressure of 185, hypertrophy of the heart, and a big liver. The urine was negative, except for bile and indican. In 1909 the blood-pressure was 190. In 1910 he had considerable dyspnea and cough, and thought he was catching cold too easily. In spite of emphatic advice to take a rest or prolonged vacation, he stuck to work. In February, 1911, there was more dyspnea and another supposed laryngeal cold, which caused aphonia before he saw a physician. The blood-pressure then was 200, and physical examination and the x-rays showed much cardiac hypertrophy and enlargement of the aortic arch. There was paralysis of the left vocal cord. Aneurism seemed certain and the prognosis bad. He was treated by absolute rest, scant foods and drink, and hot tub baths and mild sweats almost daily. Small doses of iodides were used for many weeks, and nitroglycerin in one to ten-drop doses every hour were tolerated for days at a time, and seemed very beneficial. On account of constipation, bile and indican, and sometimes albuminuria with casts, alkalies were used constantly and freely. Vichy, magnesia,

Carlsbad powder, soda bicarbonate and vegetable cholagogues, urotropin and salicylates were used at times. Bromides and small doses of chloral were taken frequently with much advantage. The blood-pressure gradually dropped to 150 and later to 130. After twelve weeks' rest in bed his voice began to return and the x-rays showed a much smaller heart and aortic arch. Since that time the patient has been watched closely. He has almost retired from business, has travelled some for pleasure, and visited the European spas. He feels fine; the heart is not much enlarged, though the urine contains bile too constantly, and some albumin and casts quite frequently, and the blood-pressure varies between 160 and 200. In this case, therefore, while the blood-pressure still remains high, most of the annoying symptoms have disappeared, and of undoubted and perhaps equal value have been the medication, absolute rest, diet, hydrotherapy, and withdrawal from business activity.

CASE IV.—The patient is aged sixty-six years, and has been under observation for four years. He is a financier, manufacturer, and employs men by the hundreds. He has always lived well, not alcoholic, but not an abstainer. His maximum weight was 265 pounds, five years before. Four years ago his weight was 165 pounds, at present 218 pounds. He was never sick in bed, but gave an indefinite history of a chancre at the age of forty-eight. There were no secondaries. He had been somewhat icteric for some years, and was annoyed with dyspnea, headache, insomnia, and weakness; could hardly walk a block, and thought he would soon be in a wheel-chair. He had positive signs of tabes, though the Wassermann test of the blood was negative. The arteries were firm, and there was marked hypertrophy of the heart. The liver shows enlargement at most of the examinations, and he is always tender over the gall-bladder.

The urine occasionally shows bile or a trace of albumin or a few casts. He has been treated by injections of mercury to the point of toleration. The injections were given twice a week for periods of two months, with four-month intervals. I could never see that he was benefited by the constant use of iodides. The nitroglycerin and tetranitrate in very small doses, taken three times a day are almost intolerable. A strict diet, the routine use of alkalis, cholagogues, and frequently a five-grain pill of blue mass, together with hot baths, light massage, and some exercises, have given the patient much relief. He is stronger and can walk quite easily. The heart is smaller, but the liver is still palpable. The systolic blood-pressure has varied from 150 to 210. No doubt mercury is the remedy which in his case has been most beneficial, but of unquestionable value were the alkalis. In this case the failure to reduce the blood-pressure is perhaps not so serious a matter as one might think.

CASE V.—A housewife, now aged seventy-five years, has been closely observed for four years. She was never seriously ill, and complained only of dyspnea and a cough (bronchitis, she said), which annoyed her for several years previously. She also complained of indigestion and constipation. Her liver was enlarged, and there was tenderness over the gall-bladder. Her weight was 160 pounds. There was hypertrophy of the heart, but compensation was fairly good. The arteries were full and firm, and the blood-pressure 198. Several times during the last four years she has had attacks of pain over the heart and stomach, simulating angina pectoris, though they were more common at night. But as some of the more recent severe attacks of pain have been observed more closely, I am convinced that the patient is more likely to have a chronic disease of the gall-bladder. Bile is frequently found in her urine, sometimes considerable albumin, with a few casts, and at other times 1 to 3 per cent. of sugar. The quantity and specific gravity of the urine are usually normal. Her blood-pressure, taken frequently and under various conditions, has varied from 145 to 210 and more. When she follows most faithfully the advice about diet, drink, and exercise she usually shows a lower pressure. But a high pressure and associated symptoms are just as positive when the patient is under nervous strain, such as has been observed when there was sickness in the family or even disappointments in the affairs of her home, which is her pride. But the patient has been faithful to advice and treatment, and in spite of continued hypertension, she says she feels much better than she did some years ago. She has taken iodides and nitrites repeatedly in such small doses as she could tolerate, but excepting a few occasions it is doubtful whether such remedies have been of any value. Remedies which have been found most helpful are cathartics, cholagogues, alkalies, bromides, and digitalis, together with hydrotherapy. And though medical treatment has been of some value, it is not improbable that this patient has an underlying surgical condition of the gall-bladder.

CASE VI.—This case is that of a man under close observation for three years prior to his death, at the age of fifty-four years. Though the time of observation was but a short time ago, the patient's condition and struggle for existence deserve some report. He was a mechanical engineer, and had unusual ingenuity and business capacity. Though in comfortable financial circumstances, he possibly accumulated more wealth for others than himself. When first seen he said he had never been sick. There was no history of venereal disease nor alcoholism, and he did not smoke. Some years before he was confined to bed a few months on account of a broken leg and arm. He complained only of being weak, tiring easily, and lacking former ambition. He said he had some dyspnea, headache, and distress after meals. His

blood-pressure in the arm was 230. The pulse was firm and a little irregular, and the heart considerably hypertrophied toward the left and also to the right. The liver was palpable, the gastric contents normal, and the urine contained only a trace of albumin. Repeated examinations of his urine were made from first to last, and the findings were about as follows: Twenty-four hour quantity and specific gravity normal; occasionally a trace of albumin and a few casts were found (sometimes many casts and no albumin), but more frequently bile and indican were present. He was at once put under rather strict regimen, partaking of scant non-nitrogenous diet; a medical treatment was outlined, and there was some relaxation in his business. At the end of the first six months' treatment he said he was much more comfortable. Some of his annoying symptoms had almost disappeared. His heart showed less hypertrophy, and the liver was no longer palpable, though the blood-pressure did not drop below 200. Then in an improved condition of health, he plunged into business again when competition was most keen. He secured business orders amounting to several million dollars, sufficient to keep a large plant busy for two years in advance. And though he won his laurels, he paid a dear penalty for such intense application. Emerson's maxim that "everything costs" is true in health as well as in finance. His former symptoms became more annoying than ever, and the blood-pressure returned to 225 and more. He found it almost impossible to partake of nitrites and iodides even in small doses. They caused unpleasant symptoms and intense headaches. However, careful dieting, hot baths and the bromides, and saline and mercurial cathartics gave some relief and comfort. He was finally persuaded after eighteen months to get away from his business for a long vacation, something which he had not taken for the previous eleven years. He spent a winter at the seacoast, and in addition to medical treatment he took a prolonged course of treatment with electricity, the high-frequency current. Before going to the coast his blood-pressure ranged from 225 to 250, but dropped to 200 soon after a little rest there.

The physician applying the electricity reported favorably at first, stating that he soon found the pressure as low as 175, and daily treatments reduced it to 155 and 160. But when the patient returned to the city to meet a business appointment, after a few months' treatment with electricity, I found the pressure as high as 235; so he returned to the coast for the remainder of the winter, but he failed to show any improvement for some time. Early in the spring he attempted to resume some work without seeking further medical advice, but a severe nose-bleed in his office and at his home brought him under observation again. Then after much disappointment and great anxiety about business again,

I found him intensely weak, dyspneic, without appetite, and unable to sleep. The pressure then went to 240 and 260. The heart was larger than ever, and there was a marked aortitis and dilation of the aortic arch, a condition confirmed by able consultants and x-ray examination. From that time until five months later, when he died, he was treated by diet, packs, iodides, vasodilators, cathartics, sedatives (in insufficient quantity perhaps), and digitalis at times. Frequent venesection gave some relief for a few days, though the patient several times became delirious, even almost maniacal for several days after the withdrawal of twelve ounces of blood, and the blood-pressure would not remain below 200 for more than a few days.

He became more restless than ever and made a desperate struggle for a recovery which he thought ought to come soon and completely. But attacks of angina pectoris developed and continued to the end. It should be added that this patient, respected by everyone, was of such a temperament that he was his own worst enemy. He was an indefatigable worker, and though kind to everyone, he was irritable under heavy pressure. He could not undertake anything without throwing the last spark of energy into it. He could not surrender to ideas differing from his own without positive conviction. Any subordinates in his employ or any members of his household who failed to meet his expectation were a source of worry and disappointment.

Hypertension and constitutional disease resulting in death should not be surprising when one considers such a nervous disposition and constant application through eleven years without a vacation.

DISCUSSION. The literature on hypertension is now becoming voluminous, but opinions expressed by thoughtful and capable men are so much at variance that one is perhaps excusable for doubting a great deal that is said. Much that is written may be classified and placed under one of three subdivisions:

1. Under the first is seen the experimental, largely technical and almost ultrascientific work, though even this is not free from the theoretical.
2. In the second is much report of practical experience, though combined with empiricism.
3. Under the third are dogmatic statements, interesting but of questionable significance.

Up to the present men are no more of the same opinion about hypertension than they were years ago in the study of other pathological conditions. Not many years ago a diseased ovary was almost routinely and perhaps often unwisely subjected to operation; appendicitis was a subject causing vicious argument and bitter criticism; and many recognized heart lesions were either favored or hampered by aconite or digitalis. So at

present many opinions about the etiology, prognosis, and treatment of hypertension are not conclusive either. Too frequently the mere mention of hypertension is considered a sequel of alcoholism or syphilis, and is coupled with the name of some drug considered a vasodilator and a specific remedy. But not until one knows that vasodilators are no more of a specific in hypertension than is digitalis in all forms of heart lesions, can he appreciate the cause of failure to restore the abnormal condition. A specific treatment is out of the question where a specific cause is unknown. And the supposed causes of hypertension are about as numerous as the causes of headache, likewise the prognosis is about as uncertain as life itself. And the methods of treatment are, and perhaps should be, widely different. How frequent are disappointments after the routine use of iodides and nitroglycerin. And how disappointing are the many brands of buttermilk for the prevention of senility. The elixir of life and perpetual youth is still a fable in spite of remarkable statements.

ETIOLOGY. Though pathologists agree on postmortem tissue changes, they after all see that different lesions in different organs produce a common group of symptoms with an equal amount of tension. And though there is much agreement about the pathology, there is a contrasting disagreement about the etiology, prognosis, and treatment. In spite of the opinion that some toxin circulating in the blood causes first a contraction and later pathological changes in the vessels to produce hypertension, no such specific poison or poisons have been recognized. Opinions expressed about the probable nature and source of such a toxin are many, and the failure to find it is a disappointment. But the same is true of many other afflictions. However, as the effect of certain known poisons, such as metals, when introduced into the system, is unquestionable, some conjecture about the effect of indefinite poisons developing within through the imperfect functions of various organs must be permitted. The toxic symptoms caused by bad hygiene, disorder of the ductless glands, as well as the disturbed function of the kidneys, heart, and entire digestive system, are so positive, that none can fail to recognize them. Indeed, such a failure is inexcusable. Of course, there is no plausible explanation known at present why the toxins caused by disease of these various organs produce hypertension in some patients and not in others. But such is the case. In thyroid disease we have a striking example. The low pressure found in that condition is very common and not surprising, but it may also be very high. A patient with alarming symptoms of hyperthyroidism, even of suffocation from the pressure of a large gland demanding immediate operation, has been under observation for several years, and has had hypertension both before and since his thyroidectomy.

To recognize any abnormality of the blood is imperative, and a positive knowledge of elimination from the bowels and skin is most essential. To examine urine for sugar and albumin without regard for the presence of other poisons as bile and indican, and the microscopic findings, as well as for the twenty-four-hour quantity, is equally inexcusable. Nor should the influence of the infectious diseases, syphilis and other venereal diseases, be overlooked. Though perhaps fully as important as anything else is the influence of the nervous system upon hypertension. Many of these patients live and work under such great mental strain and nervous tension that, if it could be measured, it would probably even surpass the arterial tension. Consequently, while there is much conjecture about the etiology, it must be emphasized that any failure to search for the most probable cause of hypertension as well as a disregard for the associated symptoms and physical signs, makes the treatment of the condition much less irrational.

PROGNOSIS. While the prognosis in any case of hypertension may be difficult, it is frequently demanded. Surely no statement should be made to patients without great caution and due appreciation of all annoying symptoms. To presume that the condition becomes the more serious as the tension is higher is a common error. And whether the tension be moderately or extremely high and whether the associated symptoms be mild or severe, a hopeful outlook, except in rare instances, is the only one to give a patient. Numerous cases similar to the ones above reported convince me that when prognosis is based on the following conditions it is very frequently correct.

1. Where hypertension exists with but little or no recognizable disturbed function of other organs the outlook is the most favorable.

2. Where it is associated with marked disturbance of any one other organ alone it is more serious.

3. Where it is associated with great defect of several other organs, such as kidney insufficiency, cardiac insufficiency, cirrhosis of the liver, and lesions of the gastro-intestinal tract, the prognosis is most serious.

4. When the hypertension is associated with symptoms and physical signs which disappear after a more or less active and prolonged treatment, which, however, fails to lower the tension, a favorable prognosis is not unwarranted. Such cases are rather frequent, and I believe it is just as unreasonable to take an unfavorable view of them as it is to predict a speedy fatality in all cases of pulmonary tuberculosis where the bacilli are found in the sputum.

5. When the tension is found in connection with changes in organs producing such extreme symptoms as dropsy, ascites, cyanosis, and orthopnea, and when these symptoms cannot be relieved whether the tension is modified or not modified by heroic

treatment covering five to eight weeks, then defeat is sure. And the extraordinary measures, such as drastic purging, venesection, and medication, with excessive doses, are entirely useless, or effectual only for a short time, and sometimes more cruel than humane.

Thus two patients with hypertension the result of cardiac, vascular, and renal disease were under observation at the same time in St. Luke's Hospital. Both had much dyspnea and dropsy; one patient also had ascites and a big liver.

After several weeks of active treatment in a futile effort to restore health, these patients, though considered incurable when first seen, were relieved of much dropsy, and the blood-pressure was lowered to points between 140 and 160. One morning both patients were found weak and extremely delirious, possibly on account of cerebral anemia, the result of a relatively lower blood-pressure in the head than in the extremities. They were given more food and some stimulants or tonics, and their delirium disappeared in a few days. One died suddenly of angina pectoris after a few weeks, and the other of cardiac insufficiency several months later.

The belief that there are different degrees of tonus in the different parts of the body was first mentioned by Hoover a few years ago. No doubt a more general recognition of this condition, whether made by the hand of the examiner or by the instrument, would be helpful in the treatment.

TREATMENT. A lengthy discussion of the treatment of hypertension is not the aim. Though the success or failure to modify the blood-pressure in the six cases here presented, to which a report of great numbers could be added, is quite convincing that no routine method can be followed. The too frequent use of the sphygmomanometer, with a report of the pressure, is bad policy and positively harmful to many anxious patients. A little diplomacy or an evasive answer, with the assurance that it does not matter particularly, is good psychotherapy. Now, while the literature contains many good suggestions, it also contains many that are worthless. But this is sure, where it is impossible to prevent the accumulation of toxins there must be constant elimination either through the organs of excretion or by withdrawal of a part of the blood containing them, or they must be made more harmless with some form of medication. Elimination through the skin, kidneys, and bowels is a common procedure, the methods differing only according to individual opinions. Removal of the cause is, of course, old advice and essential. Where there is an underlying specific disease, which can be met by specific treatment, any other treatment is of secondary consideration.

Since Fischer, of Cincinnati, and others have studied the influence of alkalies upon the blood and the kidneys, I have used

the remedies much and with undoubted advantage. Even before that time I was impressed with the benefit derived from the alkalies prescribed for many cases of hypertension in whom there was an impaired function of the kidneys, liver, and bowels, and especially in many cases of gastric hyperacidity. Of course, various methods and medicines have their adherents, and it is not the intention to underestimate the value of vasodilators, iodides, and alteratives, and even various tonics, which have their place according to indications. Rolleston has reported much benefit from the use of urotropin, salicylates, and vaccines for the toxemia of digestive disturbances. He reports especially good results in those cases of chronic disease of the gall-bladder, which either do not require or do not submit to operation, as well as in cases which have not been cured by operation. Chronic toxemia and subsequent hypertension following prolonged disease of the gall-bladder, appendix, or general digestive system may be hard to believe, but fully as hard to deny. And though the term "gastro-intestinal auto-intoxication" may be vague, it must not be forgotten. The value of frequent venesection and perhaps even the emetics used in former years is not sufficiently appreciated. The administration of thyroid extract has only been disappointing, and the high frequency current of electricity is far from giving general satisfaction. Sedatives, such as asafetida, bromides, small doses of veronal, chlorotone, chloral, and even codeine, combined with phenacetin, have been of greatest benefit; and while sedatives must be used with caution it is not always best to withhold them absolutely or too long in desperate cases. Anyone will be impressed with the change in pulse and lowered tension produced through the night by the administration of a cathartic and a small dose of opium or an equally small hypodermic of morphine.

Diet, of course, is no less important than medication, but so often foolishly restricted; and while overfeeding must be prohibited, a diet of buttermilk is not a specific nor sufficient for prolonged treatment. Personal habits must be faultless. Rest, exercise, and hygiene must be carefully directed and respected. A partial and sometimes entire withdrawal from business, or a radical change of occupation as well as change of environment and climate, all may be necessary. Domestic infelicity is a serious barrier to successful treatment. Any nervous strain from overwork and from worry, so often needless, must be relieved.

While hardening of the arterics and high blood-pressure are not necessarily coincident with advancing years nor the index of senility, so commonly supposed, the association of high vascular tension and great nerve tension is a common observation. Accumulation of wealth is often at the expense of health. "Better a handful with quietness than both hands full with travail and

vexation of spirit," is good philosophy for health and prevention of disease. Though it is hardly safe to presume that there is a relatively low blood-pressure in the wealthy indolent, the so-called nobility, nor even in the individual of leisure enfranchised by the War of the Rebellion.

A reputation for laziness would be considered as infamous slander by five of the cases herein reported. Only the one who was never known to hurry has the assurance of extreme age.

A report of most excellent health in these patients is often followed by sudden exertion or haste resulting in sudden apoplexy or death. The patients who cannot realize the wisdom of deliberation are numerous and hard to manage. For many of these there is some relaxation in books such as the story of *Napoleon Jackson*, the negro, likewise some of the works of Mark Twain, and *Adventures in Contentment and Friendship*, by Grayson. Such recommendation of books has been followed by good reports not attained by medicine.

And happy is the patient who has secured mental peace through such philosophy as Bryant has put into the last paragraph of "Thanatopsis;" but pitiable is the other patient, who, fearing the end of life and apprehensive of sudden death, is miserable to the last moment.

THE ELECTROCARDIOGRAPH AS A CLINICAL INSTRUMENT.¹

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For the skilled cardiologist there is nothing new offered in this paper. For the practitioner who has waited to see if the electrocardiograph would prove a useful clinical instrument there may be desired information. Some five years of experimental and clinical work conducted by various investigators has afforded facts the consideration of which proves the usefulness of the instrument.

About 1856 Kölliker and Müller demonstrated that each contraction of the heart generated electric currents like any contracting muscle. These currents are minute, and it was only about 1900 that Einthoven, a Dutch physiologist, perfected a galvanometer sufficiently sensitive to record them accurately and quickly.

Briefly the electrocardiograph consists of a delicately silvered quartz or glass string 0.002 to 0.003 mm. in thickness, suspended between the poles of the galvanometer by a carrier and attached

¹ Read before the College of Physicians of Philadelphia, November 5, 1913.

by wires to the electrodes leading from the patient. Between the patient and the instrument is a switch-board with several keys whose function is to protect the string, compensate for skin current, bring in or throw out of circuit the body, calibrate the excursion of the string, select the proper lead, etc. The delicate string is magnified by a microscope, and its shadow, vibrating with each heart-beat, is projected by an arc light through the microscope upon the slit of a camera containing a plate or a film moving at a fixed rate and at the will of the operator.

We will briefly review the theory of the electrocardiograph and the electrocardiogram of the normal heart contraction that we may understand the abnormal curves:

Electrodes attached to the patient's extremities will lead off these currents to the galvanometer just as accurately as if the heart were exposed and the electrodes applied directly to that contracting viscus.

That these curves arise from the heart contractions is demonstrated by the fact that the curves obtained by the electrodes attached to the extremities, or attached to the intact chest walls immediately over auricle and ventricle, or attached to the auricle or ventricle laid bare, are all the same. Since the patient has only to lie or sit with his hands and a foot resting comfortably upon the electrodes covered with absorbent cotton, wet with a solution comfortably warm, every sufferer with cardiac disease is not only willing but anxious to lend himself for the study of his malady.

Thus on one hand we have the willing patient for direct examination, instead of drawing parallels between him and the experimental animal, and on the other hand an instrument so sensitive that every heart-beat, no matter how rapid or irregular, is recorded with mathematical precision. Certainly one of the few examples where a branch of medicine is reduced to an exact science.

We cannot as yet explain all the deflections in the electrocardiograms from a presumably normal heart. However, there are variations which are within the limits of health and still further variations which place the individual among the abnormal. It is the measurement of the direction, duration, and time relationships of the events in these curves which forms the basis of electrocardiography. The curves given as normal are the result of the examination and a comparison of a series of curves from a group of healthy individuals. In a large group of presumably normal people there is likely to be found an abnormal curve or so, and a careful examination of the individual will reveal slight abnormalities of the heart never suspected before.

The curves for any given person are constant at all times; so much so, that they have been suggested as an added means of identification of the individual. Any marked deviation from one's particular curve means a deviation in function. Given a normal

curve, we can predicate that the auricular contraction began at the pacemaker (sino-auricular node) and followed the usual course through the auricle; and further, that the normal ventricular complex shows that this impulse reached the ventricles by way of the auriculoventricular bundle, its main branches and their ultimate subdivisions, for it has been demonstrated repeatedly, experimentally, and clinically, that the character of an electrocardiogram, like the curve from a contracting strip of plain muscle, depends upon the point of origin and the direction of the current in the heart.

More often all graphic methods in heart disease are most useful in differentiating the arrhythmias, but the electrocardiograph also yields definite and often unexpected information derivable by no other means in some conditions where the rhythm is *regular*. For instance, there are certain deviations in the directions of parts of the curve, representing each beat, where the rhythm is perfectly regular, that clinical experience has shown to be of bad prognostic significance. Mitral and pulmonary stenosis are cardiac abnormalities which produce clear symptoms and physical signs.

They should be, and postmortem shows that they are, accompanied by the expected right-sided ventricular hypertrophy. Such cases yield characteristic but abnormal curves. That such curves are characteristic of right-sided ventricular hypertrophy is also rendered likely from the following fact: Relative preponderance of the right ventricle is normal in the infant for the first few weeks after birth. Curves of such infants show the same characteristics referred to and keep them until the second or third month, when the child assumes the normal adult form.

The curves of left ventricle hypertrophy show deflections in exactly the opposite directions to those of the right side. We should expect to find these characteristic curves of left ventricular hypertrophy in aortic valve disease, nephritis, arterial sclerosis, and any disease with a constant high blood-pressure. As a rule we do, but they are by no means as constant where expected as are the characteristic curves on the right side.

These abnormal curves on the left side are often absent when expected and appear when not expected. Many electrocardiographic findings and clinical comparisons serve to emphasize the facts that the physical signs which aim to differentiate right- and left-sided ventricular hypertrophy are not always reliable, that increased fluid pressure within the ventricle from an incompetent valve is far from explaining all cases of hypertrophy, and that on postmortem the distribution of increased muscle tissue is not always where expected.

There are evidently factors in hypertrophy which are as yet little understood, but there seems no valid objection to adopting the suggestion of Lewis to speak of right- and left-sided preponderance where these characteristic curves occur. Furthermore, these curves

when sufficient electrocardiographic and postmortem material from the same cases are collected, may help throw more light upon the subject.

We cannot repeat too often that a normal electrocardiogram means that the impulse arose in a supraventricular focus, and followed the normal pathway, the auriculoventricular bundle, throughout all its ramifications to and throughout the ventricles.

Again, the electrocardiograph alone reveals contractions which arise in a supraventricular focus, but follow an abnormal course to the ventricle, the so-called *aberrant* contractions.

For instance, if the left main branch of the auriculoventricular bundle is permanently or transiently deficient the impulse is entirely deflected to the right side of the heart, and though eventually both ventricles contract, the curves of such contractions are abnormal. They partake partly of the nature of the curves of right-sided preponderance or of stimulation near the base of the right ventricle.

If the right main division of the auriculoventricular bundle is deficient the impulse is carried to the left ventricle and the curve simulates the curves of left-sided preponderance and apical stimulation. Though these curves of aberrant contractions simulate the curves of preponderance, the two are fairly easily distinguishable by exact measurement. The only physical signs in a patient with aberrant contractions may be the presence of reduplicated first sounds and some enlargement of the heart on percussion.

The electrocardiograph alone reveals these defects of the main divisions of the bundle. Where this condition is permanent a main stem of the bundle is probably involved in a fibrotic change surrounding it: It is frequently associated with the auriculoventricular heart-block. Right bundle defect is the commonest, and it is most frequently associated with aortic disease.

It may be found that there is an anatomical reason, and the aortic valve and ring thickening may cut off the blood-supply more often to the right ventricle. This condition is of bad prognostic significance. Where temporary it suggests acute involvement of the bundle branch by toxins and bacteria. Lewis has recorded rheumatic cases when the condition cleared up as the fever subsided. Here we have definite evidence of myocardial involvement and an explanation of slight fever explained in some cases by no other means. A galvanometric examination of the functions of the cardiac muscle in rheumatic and other febrile diseases would probably often show that we frequently put patients to bed too late and allow them around too early.

A comparison of our knowledge of the cardiac arrhythmias a decade ago with the wealth of known facts is a glowing tribute to the polygraph, the electrocardiograph, and the workers with these instruments.

Irregularity of the heart's action has been shown to be a complex

subject, and yet capable of being resolved into several more or less simple varieties by these instruments of precision. Moreover, the fixing of these definite clinical entities has added much to our prognostic and therapeutic knowledge of heart disease.

The cardiac irregularities are included under the following heads: auriculoventricular block, extrasystoles or premature beats, simple paroxysmal tachycardia, auricular flutter, auricular fibrillation, sinus disturbances, and alternation.

The electrocardiograph depicts with mathematical accuracy any variation in the conducting function of the auriculoventricular bundle. We know that normally the impulses causing the cardiac contractions arise in the sino-auricular node (at the junction of the superior vena cava and auricle) and travel by the auriculoventricular bundle to the ventricles in at least 0.2 second. Any increase beyond 0.2 second, in this technically named *a-c* or *P-R* interval, is abnormal, and detected with the greatest accuracy by the electrocardiograph. Frequently this increased *P-R* interval, the first step in block, is the only evidence we have that rheumatism or other infective disease has involved the myocardium. With precision the instrument pictures simple prolonged conduction, dropped beats, the varying responses of the ventricle to the auricle, complete dissociation of auricle and ventricle, and finally the exact sites at which the impulses arise which control the independently beating auricle and ventricle. The same curves not infrequently show not only heart-block but right- or left-sided hypertrophy, and premature beats with the exact location of the origin. Furthermore, the slow pulse due to true bradycardia, such as occurs after infectious diseases like influenza, and true nodal rhythm are sharply defined from block.

Premature beats, the commonest cause of intermittent pulse, are shown to be ectopic in their origin, that is, they arise at points other than the sino-auricular node. Their ventricular, auricular, or junctional origin is made clear. If ventricular, the shape of the curve shows whether they arise in right or left ventricle. If auricular, their abnormal curve reveals their ectopic focus of origin, their abnormal course through the auricle; and further, the normal ventricular response shows that the impulse followed the normal path (auriculoventricular bundle) to and throughout the ventricles. Again, if the ventricular response is abnormal to this ectopic stimulation from the auricle, it is shown to be due to deficient conduction in one of the main divisions of the bundle (aberration). Premature beats are easily recognized in electrocardiograms, but in other graphic records, especially where they occur in groups, they may simulate auricular fibrillation, heart-block, flutter, and alternation.

Simple acceleration of the pulse such as occurs in fever, hyperthyroidism, after muscular exercise and emotion, are distinguished by their normal electrocardiographic curves from simple paroxysmal

tachycardia. The latter is due to an ectopic focus in the auricle catching the lead and dominating the rhythm. This focus is usually in the auricle, but occasionally in the ventricle. The electrocardiograms distinguish simple acceleration, simple paroxysmal tachycardia, and auricular flutter.

Auricular flutter, unless treated by digitalis and a higher grade of heart-block than the usual 2 to 1 produced, can rarely be diagnosed accurately except by the electrocardiograph, and that instrument alone reveals the ectopic origin of this abnormal form of heart action. Untreated, this rapid heart action tends to persist over long periods, much to the detriment of the patient with an already overtaxed heart. The good results of treatment are fully worth the trouble of an accurate diagnosis.

Auricular fibrillation demands accurate diagnosis because of its frequency and the usual brilliant results in treatment. True, it can be diagnosed often by the palpating finger, the stethoscope, or the polygraph, but slow fibrillation is easily overlooked if ordinary methods alone are used in diagnosis. The constant absence of auricular contraction variation *P*, and the presence of the oscillations due to the fibrillating auricle in the curves, the perfectly regular pulse with the auricle still fibrillating where complete block is present, the pictures of block, of aberrant ventricular responses, of ventricular extrasystoles with their different foci of origin, as in digitalis coupling, make the curves quite worth while, though the bare diagnosis of auricular fibrillation may be already made by other means. Respiratory arrhythmias and sino-auricular block are worthy of distinct separation from other irregularities not because of their clinical importance, but to allay the anxiety of the patient, and not unfrequently of the physician himself.

In alternation we have perhaps the one condition where the polygraph may give evidence not afforded by the electrocardiograph. However, on the other hand, the latter instrument sometimes shows alternation where the former fails. Recent evidence as to the grave prognostic significance of alternations makes it worthy of study.

The introduction of the phonocardiograph, by which murmurs may be registered graphically simultaneously with the electrocardiogram, should prove useful, especially in teaching the subject of heart disease. This will be more practical, since a form of electrocardiograph is appearing in which two strings may be used in the same galvanometer, one registering the heart contraction (electrocardiogram) the other the heart sounds and valvular murmurs (phonocardiogram).

In the electrocardiograph we have then an instrument which shows whether each impulse that gives rise to a cardiac contraction arises in the normal pacemaker (sino-auricular node) or elsewhere in the auricle or in the ventricle, whether the impulse pursues the normal course through the *A-V* bundle to and throughout the

ventricles, or an aberrant course, and whether the rate of propagation from the auricle to the ventricle was normal or delayed. An instrument which pictures all these facts with mathematical precision must be and is more accurate than the registration of cardiac movements by means of the polygraph, which depicts alone the changes in intra-auricular, intraventricular, and intravascular pressure. However, though the electrocardiograph will be the court of last resort, the ink polygraph, because of its portability, its comparatively small cost, and the large amount of information it is capable of providing, is in no danger of being relegated to the shelf. Again, the knowledge obtained from electrocardiograms makes easier the interpretation of polygraph curves with greater accuracy, and a knowledge of the information afforded by both instruments increases the diagnostic ability of the physician by means of the palpating finger and the stethoscope alone. The different forms of cardiac irregularity have been shown to vary widely in their prognostic significance and their reaction to treatment. In the future the patient will expect, the insurance companies will often require, and the conscientious physician will not rest satisfied without a determination of the exact character of the cardiac irregularity in question.

The increased working reliability of a good electrocardiograph, the decreased price, and the known refinements in diagnosis it affords render the possession of one necessary by every hospital trying to do the best grade of work in cardiac diseases. Since the best deflections of the string are obtained in a strong magnetic field, the electrocardiograph with a *permanent* magnet must prove its worth before its greatly reduced price should be a factor in selecting an instrument.

The writer has attempted to treat the subject in a general way. Those not already familiar with it will find the whole subject technically yet simply set forth in *Clinical Electrocardiography*, by Dr. Thomas Lewis, to whom the writer wishes to express appreciation of his work and of the opportunities to participate therein in his laboratory which Dr. Lewis has afforded those interested in the subject.

A SIMPLE METHOD FOR THE INDIRECT TRANSFUSION OF BLOOD.

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THE method consists of two parts: (1) obtaining blood from the donor, by means of an aspirating apparatus, and its defibrina-

tion by shaking in flasks with glass beads; (2) the introduction, intravenously, of the defibrinated blood into the patient.

Apparatus Required. Five Erlenmeyer flasks, each of 300 c.c. capacity, two ounces of glass beads, one infusion bottle, two infusion needles, twelve and one-half feet of rubber tubing, eighteen inches of glass tubing, one thumb-screw, one rubber stopper, with two holes, and four plain rubber stoppers.

Preparation of the Apparatus. For the aspirating outfit two pieces of glass tubing, each four inches long, are bent at the middle to form right angles; one end of each of these tubes is passed through the rubber stopper containing two holes, and to the free end of one of these tubes an infusion needle is attached by means of a short rubber connection not over one and one-half inches long. The needle should be about two and one-half inches long, and of fairly large caliber. To the free end of the other glass tube is attached six inches of thick-walled rubber tubing fitted with two inches of glass tubing to serve as a mouth-piece.

Into each of four of the Erlenmeyer flasks is placed one-half ounce of glass beads, and the flasks are stoppered with cotton wool.

The apparatus for the introduction of the defibrinated blood is made ready by attaching a small infusion needle to the infusion bottle by twelve feet of rubber tubing. This tubing is interrupted by two glass cannulæ, three or four inches long, one placed at its middle and the other about three inches from the needle. A thumb-screw is placed on the rubber tubing between the second glass cannula and the needle. All the connections between rubber tubes, glass tubes, and needles are made secure against leakage with heavy silk thread.

Sterilization of Apparatus.—The four flasks containing glass beads are sterilized by dry heat, and may be prepared in advance and kept on hand ready for an emergency.

The remainder of the apparatus, consisting of the infusion bottle with its attached tubing, needle, and thumb-screw; one Erlenmeyer flask, four plain rubber stoppers and the rubber stopper with its attached tubes and needle, is sterilized, just previous to using, by boiling.

After sterilization the rubber stopper carrying the needle is fitted into the empty Erlenmeyer flask and a little melted paraffin, which has been heated to 200° C., is aspirated through the needle into the flask, in order to coat the inside of the needle and tube to prevent the blood from coagulating there while it is being taken from the donor.

After the paraffin has been introduced, air must be continuously aspirated through the needle until the paraffin solidifies on the inner walls of the needle and tubing in order to prevent the lumen from becoming occluded. This stopper is now fitted into one of the

flasks containing beads and a little sterile cotton is inserted into the mouth-piece attached to the rubber tubing.

Obtaining Blood from the Donor. The skin over the large veins at the bend of the elbow is rendered aseptic, a muslin bandage is placed around the upper arm tightly enough to cause the veins to stand out prominently, but not so as to obliterate the arterial pulse, the needle of the aspirating apparatus is introduced into one of the large veins, and blood aspirated rapidly into the flask by means of suction applied to the appropriate tube with the mouth.

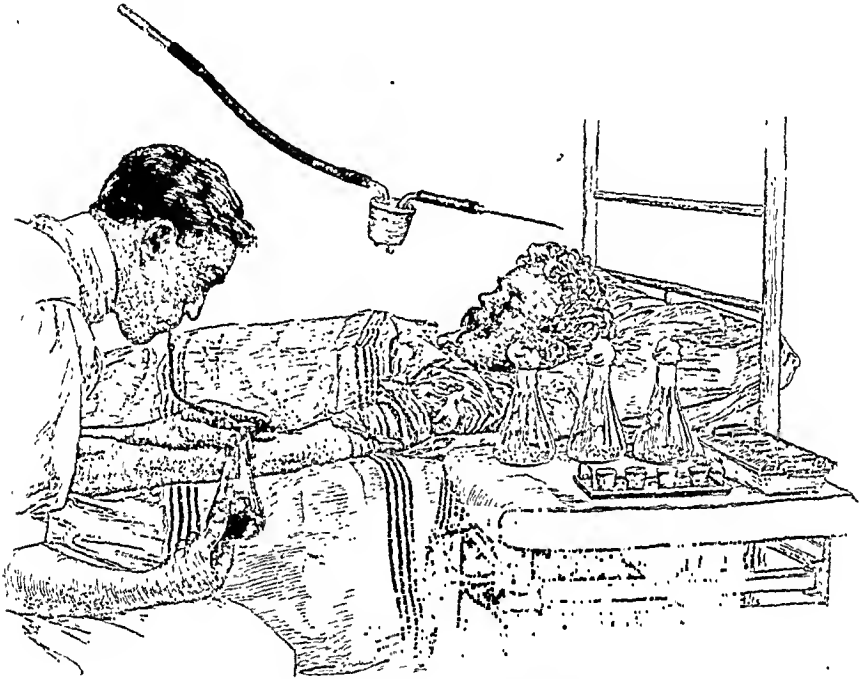


FIG. 1.—Obtaining blood from the donor.

When 200 c.c. of blood have been obtained the flask is gently removed from the stopper without disturbing the needle in the vein, another flask is substituted, and the aspiration continued as before; meanwhile the first flask is closed with a sterile rubber stopper and an assistant immediately defibrinates the blood by shaking it vigorously for ten minutes, using a circular motion. An up-and-down motion is apt to break the flask by throwing the beads violently against its bottom.

A second and a third flask of blood are obtained and treated in the same way; 600 c.c. should yield 500 c.c. of defibrinated blood.

Injection of the Defibrinated Blood into the Patient. From 300 to 400 c.c. of sterile normal salt solution are placed in the infusion bottle and allowed to fill the rubber tubing and needle connected therewith. Care must be taken to get all the air out of the rubber tubing and connections. This is somewhat difficult, and is best

accomplished by alternately raising the bottle and lowering the needle several times and then allowing the salt solution to run through the needle until only a few cubic centimeters remain in the bottle. The thumb-screw is now closed; four layers of sterile gauze are placed over the mouth of the bottle and pushed down into it a short distance to form a funnel-shaped depression; the tops of the flasks containing the defibrinated blood are then thoroughly flamed with an alcohol lamp and the blood filtered through the gauze into the infusion bottle.

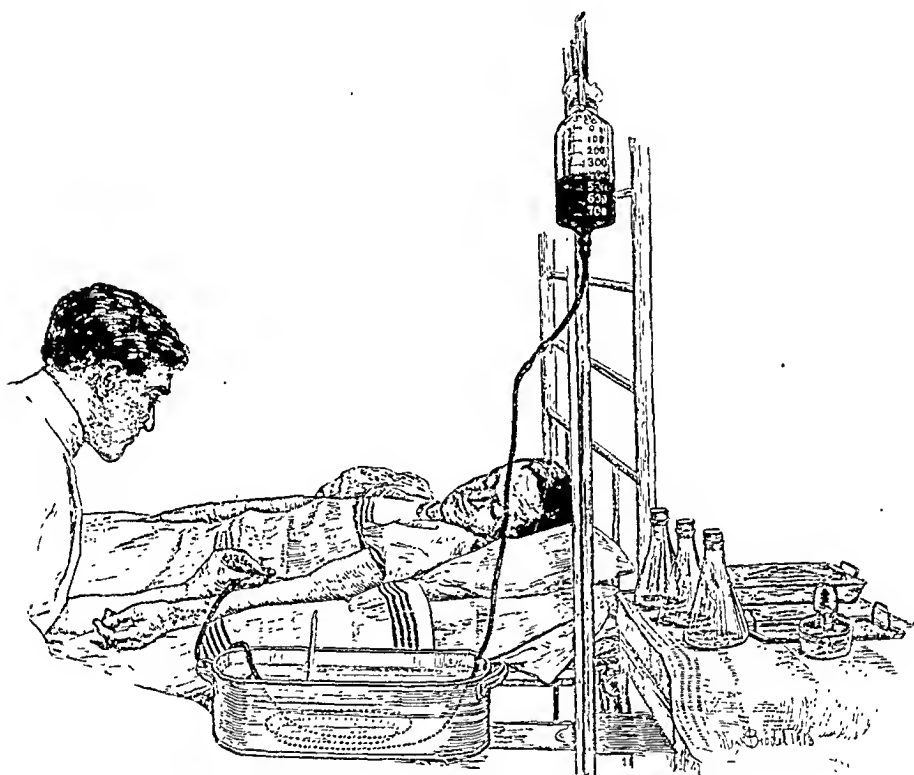


Fig. 2.—Injection of defibrinated blood into the patient.

The skin over the veins at the bend of the patient's elbow is rendered aseptic, a bandage is placed around the upper arm to make the veins prominent, the needle of the infusion apparatus inserted into a vein, and the thumb-screw loosened. If the infusion bottle has not been previously elevated, the back flow of blood from the patient into the glass cannula near the arm indicates that the needle is in the vein. The bandage is now removed and the infusion bottle elevated; the salt solution in the tubing, followed by the defibrinated blood, is allowed to run into the patient's arm.

The infusion bottle is elevated about three feet above the patient's arm and the remainder of the rubber tubing is coiled in a vessel of water placed as near the arm as possible. The water in this vessel should be kept at 38°C. , in order that the blood may enter the patient at body temperature.

The rate of flow of the defibrinated blood is regulated by the thumb-screw, so that the patient receives 100 c.c. in six minutes, the introduction of the entire 500 c.c. requiring one-half hour.

In patients with unusually small veins, especially in young children, it may be necessary to expose a vein and use a small cannula if the needle cannot readily be introduced into a vein through the skin.

Selection of a Donor. It is preferable that the donor be a vigorous healthy person of approximately normal blood count and hemoglobin percentage. It is important to rule out syphilis by a negative history and Wassermann reaction. No one having an elevation of temperature or recently convalescent from an infectious disease should be used. It is also unwise to use a nephritic patient. I have in a number of instances used as donors subjects of chronic heart disease in whom there was, so far as could be determined, no danger of infection and where a venesection was indicated on the donor's account.

It seems desirable, where possible, to select a donor who belongs to the same group as the patient, as determined by the isoagglutination reaction, in order to prevent the possibility of isoagglutination or isohemolysis. This test is easily performed and does not require more than an hour or two for its application. The method for making this determination has been reported elsewhere.¹

The Amount of Defibrinated Blood Used. The optimum amount of defibrinated blood for an adult seems to be about 500 c.c.; for children, 200 to 300 c.c.

I have given infants of two years 200 c.c., and adults 800 c.c. without untoward results, but better results may be obtained by giving smaller amounts and repeating the injection, if necessary, in from three to ten days.

General Remarks. The purpose of this communication is mainly to give the technique of the operation, but a few further statements seem desirable.

I have used it during the past three years in about seventy-five cases. It is easy to perform, although the details require careful attention, and some little practice is necessary in order to acquire facility in its use.

There are several obvious advantages over the direct method. It is much simpler of execution and certain of operation. The amount of blood transfused is under absolute control and can be measured exactly. Except in occasional cases, where it is necessary to expose a vessel, as in very small children, no scar is left with either the donor or donee, and the vessels are not obliterated.

On the other hand, one is using defibrinated instead of whole blood, which differs from the latter in that it contains a large quan-

¹ Studies on Isoagglutinins and Isohemolysins, Bull. Johns Hopkins Hospital, 1910, xxi, No. 228; also Paroxysmal Hemoglobinuria, *ibid*, 1911, xxii, No. 245.

tity of free fibrin ferment and has been deprived of its fibrinogen. Theoretically, lack of fibrinogen may detract from the value of the procedure in those cases in which the patient's blood may be deficient in this constituent. The presence of free fibrin ferment does not seem to constitute a source of danger, as the body is apparently able to withstand the injection of large amounts of fibrin ferment without harm, and in no instance have I observed intravascular clotting following the introduction of defibrinated blood.

In the series of cases transfused by the method here described there has been only one fatality which could be ascribed to the transfusion. The patient was suffering from pernicious anemia of a severe grade, with renal and cardiac insufficiency. After about six weeks of hospital treatment by the usual methods, without improvement, an indirect transfusion was tried as a last resort, and 500 c.c. of defibrinated blood were given intravenously. There was no immediate reaction, but six hours later the patient lapsed into a comatose state and died three hours after the onset of the coma. It may not be altogether fair to ascribe this fatality to the transfusion, as a week or ten days previous to the transfusion the patient had been in coma for about forty-eight hours, from which, however, he rallied.

In a majority of the cases the introduction of defibrinated blood was followed in from fifteen minutes to one hour by a chill of about a half hour's duration. This was accompanied by an elevation of temperature usually reaching 102° to 104° F., or even higher. The temperature returned to normal in a few hours, and there were no other untoward results.

The gain in the blood-count following the transfusion of 500 c.c. of blood varied between 1,000,000 and 2,000,000 cells, and subsequent observations indicated that the cells introduced live and functionate normally in the body of the recipient.

No instance of blood destruction was observed where homologous blood was used, that is, where the donor and donee belonged to the same group as determined by the isoagglutination reaction. In one instance where the donor and donee belonged to different groups, and where the serum of the donor was shown to hemolyze the patient's corpuscles *in vitro*, a transient but well-marked hemoglobinuria followed the transfusion.

It is beyond the scope of this paper to include detailed case reports; it is intended to give those at another time. The results have led me to believe that as much may be accomplished for the patient by indirect transfusion of defibrinated blood as by the more difficult direct transfusion of whole blood, except possibly in patients whose blood is deficient in fibrinogen.

The technique is published at this time in order that the method may have a more extensive trial in other clinics and in private practice.

THE ROLE OF THE CAROTID ARTERIES, IN THE CAUSATION
OF VASCULAR LESIONS OF THE BRAIN, WITH
REMARKS ON CERTAIN SPECIAL FEATURES
OF THE SYMPTOMATOLOGY.¹

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INTRODUCTION. In recent years, special attention has been given to the more exact localization of vascular lesions of the brain, and as a result a number of new syndromes have been added to the literature of this subject. The object of the present study is to emphasize the importance of obstructive lesions of the main arteries of the neck (the innominate, common carotid, and internal carotids), in the causation of softening of the brain, and more especially to urge the routine examination of these vessels in all cases presenting cerebral symptoms of vascular origin. In other words, the writer would advocate the same attitude of mind toward this group of cases as toward the intermittent claudication, gangrene, and other vascular symptoms of the extremities, and never omit a detailed examination of the main arterial stem.

Hemiplegia from occlusion of the intracranial branches of the internal carotid is one of the most frequent clinical pictures met with in medical practice, and yet apparently one of the rarest from obstruction of the main arterial pathway in the neck. However, when one considers that these vessels are frequently ignored both in clinical and pathological studies, it is not unlikely that many such conditions are overlooked.

The reason for our neglect in this respect is obvious, and springs from the assumption that the circle of Willis is sufficient to carry the blood into an obstructed vascular area when such obstruction is situated below the level of the communicating arterics. There is no question as to the correctness of this assumption in a large majority of cases, especially in young subjects with good hearts and elastic vessels. On the other hand, in those individuals with diseased and weakened hearts and sclerotic vessels, the necessary compensatory changes required for the establishment of the collateral circulation may not develop, in which event any obstruction to the direct flow of blood through the carotid artery must be a considerable menace to the circulation of blood in the affected hemisphere. In such a case, even if the collateral circulation becomes established, it may prove insufficient for the needs of the hemisphere, because of the reduction in force and the consequent slowing of the blood current, when breaking down.

¹ Presented at a meeting of the American Neurological Association, June, 1913.

would follow in that portion of the brain commonly involved in failing cerebral circulation; the subcortical white matter, and the region of the basal ganglia. It is also obvious that even if actual softening does not occur, symptoms of diminished functional activity may follow with the characteristic picture of cerebral intermittent claudication.

We also know, that entirely apart from a weakened heart and arteriosclerotic vessels, obstruction of a carotid may produce permanent hemiplegia because of inadequate arteries of communication in the circle of Willis or other vascular anomalies.

It may be well to say, in this connection, that the focus of softening found at autopsy may be merely the breaking down at the distal portion of the arterial tree, where the circulation is weakest, exactly as in senile gangrene of the extremity; the important obstruction to the blood current being situated in the main trunk. Occasionally an area of softening in the region of the central ganglia is found with the vessels of the circle of Willis soft and patulous (Hunt²). In such cases the main artery of the neck may well come under suspicion, and should be carefully examined. The same is true of embolism, in which a central area of softening is found without demonstrable occlusion of the middle cerebral. In such cases it is usually assumed that the embolus has been broken up and undergone absorption. This explanation, however, is not always satisfactory, when the vessel is patulous and evidences of secondary thrombus formation are absent.

It would, therefore, seem proper in all cases with cerebral symptoms of vascular origin, to examine the pulsation of the carotids in the neck as possibly throwing some light on the source of the obstruction and rendering more exact our localization of the seat of the trouble in this group of cases. For this purpose a section of the carotid artery is readily accessible to palpation, extending from the lower border of the thyroid cartilage to the angle of the jaw; the main trunk divides into the external and internal carotid at the level of the hyoid bone, and the internal, the larger of the two vessels, is readily felt from this point to the angle of the jaw.

The writer has examined a number of cases during the past few months, at different ages, and suffering from a variety of diseases, and in all of them has found the force of the pulsation in these vessels to be practically equal on the two sides. The only exceptions noted were in a small series of hemiplegic cases of vascular origin, in which a definite and distinct *weakness of the carotid pulsation was noted on the side corresponding to the cerebral lesion*. These cases will be referred to later. It may be well to mention that rarely congenital inequalities in size may occur, and one carotid may even be absent as an extremely rare anomaly.

* The Chronic Progressive Softening of the Brain, AMER. JOUR. MED. SCI., June, 1906.

The symptomatology of occlusion of the common carotid artery is based largely on the study of those cases in which ligation was performed, an operation formerly much in vogue for a variety of indications. There are, comparatively speaking, only a few recorded cases of carotid obstruction from endarteritis, thrombosis, and embolism, and of these not a few were associated with aneurysmal dilatation of the arch of the aorta or its branches. We will review briefly these various groups of cases in order to show the different types of cerebral manifestations which may result when the main artery is occluded, and which, after all, is only a *resume* of clinical pictures with which we are perfectly familiar, and associate with the usual softening processes of the brain, but which are rarely considered as having a possible relation to the carotid artery in the neck.

AFTER-EFFECTS OF LIGATION OF THE COMMON CAROTID ARTERY. Ligation of the common carotid artery may produce merely temporary cerebral symptoms, such as unilateral headaches, vertigo, dilatation of the pupil, transient motor and sensory disturbances, which pass away as the collateral circulation becomes established. These are the so-called *immediate* symptoms, and in this group of cases, fortunately a large one, no permanent damage to the brain tissue results.

It would be interesting to know the subsequent cerebral histories of such patients, especially in the later period of life, when the degenerative changes in the circulatory system take place, and if the one hemisphere is more predisposed by reason of defective circulatory conditions to degenerative changes; but I am aware of no investigations bearing on this question.

The so-called *late* or permanent cerebral symptoms which come on after ligation, are the result of organic changes and vary in frequency in the statistics of different observers.

Pilz,³ who collected and analyzed 520 cases in 1868, found that hemiplegia resulted in 50 cases.

LaFort's⁴ statistics, published in 1875, were based on 370 cases, of which cerebral accidents of various kinds were noted in 100.

In Nieten's⁵ series of 143 cases published in 1893, cerebral lesions occurred in 27 cases.

In Lestelle's⁶ more recent study of 126 cases, cerebral lesions were noted in 11 per cent.

It must be remembered that all of the cerebral accidents cannot be attributed to the vascular occlusion, as other factors such as sepsis and meningitis are to be considered, but some idea of the uncertainty attending the establishment of the collateral circula-

³ Zur Ligatur der Arteria Carotis Communis, Arch. f. klin. Chir., 1868, Band ix, S. 257.

⁴ L'Artere Carotid, Dict. Encyclop. des Sciences Méd. de Dechambre, 1875, T. xii.

⁵ Inaugural Dissertation, Rome, 1893. (Cited by Lestelle.)

⁶ Des Accidents Cerebraux consecutif a la ligature de l'artere Carotid Primitive. Thèse de Paris, 1903.

tion may be obtained and the dangers to the cerebral circulation from obstruction of the main arterial pathway.

The late manifestations consist usually of hemiplegia with or without hemianesthesia, aphasia, convulsions, and the other well-known symptoms resulting from obstruction in the distribution of the middle cerebral artery. Occasionally, blindness or even destruction of the eye may follow on the side of the ligation, from impairment of the circulation in the ophthalmic artery. This is an interesting symptom, and will be referred to later as a diagnostic sign of possible importance.

Before leaving the subject, mention must be made of those cases in which ligation of the carotid has been performed on both sides without ill effects, providing sufficient time has elapsed for the proper establishment of the first collateral circulation, which then conducts the blood to the brain after the second ligation. These cases show what an extraordinary power of adjustment is sometimes possible in the cerebral circulation. It is, however, by no means a certain mechanism, and in a given case one can never foretell what may be the effect of the ligation on the cerebral structures.

THROMBOSIS OF THE CAROTID ARTERY FROM INJURY. The carotid artery may become thrombosed after injuries to the neck, such as stab wounds, gunshot wounds, and the like.

The following cases have come under my personal observation, and are reported for their symptomatological interest:

CASE I.—A man, aged thirty-two years, was brought to the Hudson Street Hospital on September 31, 1903, immediately after receiving a stab wound on the left side of the neck. There was a small puncture wound in the middle of the left side of the neck, over the sternocleidomastoid muscle, from which there was practically no bleeding. At the site of the wound there was a soft swelling about the size of a pigeon's egg, which was pulseless and yielded no bruit. The patient was conscious and able to tell the history of the accident. Immediately on being stabbed he fell to the ground with vertigo, faintness, and numb feeling on the right side. On admission to the hospital, immediately after the accident, symptoms of right hemiplegia were already apparent.

On October 5. I made an examination at the request of Dr. Stimson. The man was somnolent and apathetic. His pupils were equal and reacted to light. The right side was completely hemiplegic, with considerable loss of sensibility extending to the middle line. The tendon reflexes were present. The abdominal and cremasteric reflexes were abolished on the right side. Babinski phenomenon were present on the right side. There was moderate conjugate deviation of the head toward the left side. The left temporal artery was pulseless. On the right side distinct pulsations were palpable.

Ophthalmoscopic examination shows the left papilla to be pale, the veins moderately full, and the arteries distinctly smaller and less prominent than on the right. The heart sounds were good; pulse, 72; temperature, 101°. The diagnosis of thrombosis of the common carotid artery was made.

October 6. Operation. An incision was made along the left sternocleidomastoid muscle. After a small blood-clot had been removed, the jugular vein was found punctured and was ligated. The common carotid artery was almost completely divided just below the bifurcation and was the seat of a firm thrombosis. The artery was ligated above and below the injury and the severed portion removed.

In the course of the next few days, the patient became gradually more stuporous, and terminal pneumonia developed, with rising temperature, death occurring thirteen days after the injury. The brain could not be examined.

CASE II.—A boy, aged fourteen years, was brought to the New York Hospital, immediately after an injury, on April 30, 1909. He was in an unconscious condition, paralyzed on the right side, and bleeding profusely from a punctured wound on the lower lip and floor of the mouth. He had been injured by falling from a fence upon the iron tip of an umbrella, which entered the left side of the lower lip, passing through the floor of the mouth. According to bystanders he was able to rise, but almost immediately fell to the ground, unconscious, where he remained until picked up by an ambulance surgeon a few minutes later.

Examination, at the request of Dr. Hartley, May 1, 1909, 2 P.M. In addition to the punctured wound of the lip and floor of the mouth there is a swelling beneath the left sternomastoid muscle, just below the angle of the jaw, which does not pulsate. He is unconscious, but can be aroused for brief periods, and is then irritable and somewhat resistant to examination. There is a complete right hemiplegia with diminution of the pain sense on the right side. The right knee-jerk is absent, the left present; both Achilles-jerks and the arm reflexes are present. Babinski present on the right side. Abdominal and cremaster reflexes present on both sides. Pupils are equal and react to light. Heart is normal; systolic blood-pressure is 115 mm. He vomited several times during the day. Temperature, 101°; pulse, 116. Lumbar puncture was performed and three drams of clear fluid remained, which was entirely negative.

May 2. The patient is unconscious, and cannot be aroused. The swelling on the left side of the neck is soft and baggy, and has increased slightly. It does not pulsate. There is neither rigidity of the neck nor conjugate deviation of the head or eye. Pupils are still equal and react to light. There is no pulsation in the left temporal artery. Paralysis and reflexes are as noted in first examination.

Ophthalmoscopic Examination. The arteries of the left disk are smaller than those of the right, and do not pulsate. The veins are somewhat fuller on the left side. The left papilla is distinctly paler than the right. Death occurred May 2, at 10.30 P. M.

Autopsy Note. The carotid artery of the neck was dissected out and found to be punctured at the bifurcation, and completely thrombosed. The examination of the brain showed some swelling of the convolutions over the parietal and temporal region, and the subjacent white matter was softened and broken down. On opening the corpus collosum, the floor of the left lateral ventricle was found irregularly mottled and soft. The circle of Willis was free except for thrombosis of the middle cerebral artery. Both the anterior and posterior communicating arteries were present and patulous.

Remarks: These cases are similar in etiology and symptomatology, and are of interest in the present discussion, as showing the development of immediate cerebral symptoms after puncture wounds of the carotid artery. No doubt this was due to the sudden interference with the cerebral circulation on the wounded side. It is hardly possible that embolism could have occurred so promptly. The steady advance of the softening process terminating in death, was probably due to a slow extension of the thrombus into the cerebral vessels, and which could be demonstrated in Case II. It is to be noted that in both cases there was an absence of pulsation in the temporal artery on the affected side, showing that the external carotid artery was occluded. I would particularly emphasize the slight and distinct vascular changes in the optic disk on the side of the injury present in both of the cases. Such milder disturbances of the circulation in the optic disk as well as optic atrophy, which sometimes develops, may serve to throw light on the localization of the obstruction, showing the lesion to be situated below the ophthalmic branch of the internal carotid.

PRIMARY THROMBOSIS OF THE CAROTID ARTERY (Arteriosclerosis, Endarteritis). Spontaneous thrombosis of the carotid from disease of the vessel wall occurs but rarely, and there are but few cases recorded in the literature of this subject. Among the earlier writers, cases were described by Chevers,⁷ Gull,⁸ Todd,⁹ Savory,¹⁰ and Crisp,¹¹ usually as a complication of aneurysm of the arch of the aorta or its larger branches. A more recent case of this nature has been recorded by W. Erb, Jr.¹²

⁷ Effects upon the Cerebral Circulation of Obliteration of one Common Carotid Artery, London Gaz., i, new series, p. 146.

⁸ Case of Occlusion of the Innominate and Left Carotid, Guy's Hosp. Rep., 1855, i, 12.

⁹ Med.-Chir. Trans., xxvii, 301.

¹⁰ Ibid., 1856.

¹¹ Cited by Pilz. Arch. f. klin. Chir., Band ix, S. 403.

¹² Ein Fall von Ausgedehnter Gehirn erweichung bei totaler Obliteration der Carotis Communis Sinistra, Münch. med. Woch., 1904, li, 947.

Kussmaul¹³ has also described two cases of spontaneous and gradual occlusion of the carotid. One of endarteritis, with complete thrombosis of the vessel, in which the only symptom noted was headache, and a few days before death, visual disturbances. In the second case the left common carotid was occluded and the external carotid was pulseless. The symptoms produced were left-sided headache, vertigo, and epileptiform attacks. The left optic disk was pale, the veins full, and the arteries small. There was no paralysis. He notes that the communicating arteries were but poorly developed.

In Penzoldt's¹⁴ case of thrombosis of the right carotid artery the initial symptom was sudden blindness, the sight of the right eye remaining permanently defective and the disk atrophic. Later a left hemiplegia developed. Autopsy showed complete thrombosis of the right common carotid, with a large area of softening in the right hemisphere. The external carotid was free from thrombosis formation.

Another case of optic atrophy, with contralateral hemiplegia from occlusion of the carotid, is recorded by Guthrie and Mayou.¹⁵ The left carotid was pulseless and the obstruction may have been due to embolism, as the heart action was irregular and a systolic bruit was present.

It is important to remember that symptoms of chronic progressive hemiplegia may follow thrombosis of the carotid artery. Cases of this nature have been described by Oppenheim,¹⁶ Trenel¹⁷ and Brissaud.¹⁸

In Brissaud's case, a man aged forty-seven, developed gradually the symptoms of hemiplegia, and died in coma. The autopsy revealed a large area of white softening occupying the inferior two-thirds of the Rolandic area, which had a special edematous character. The internal carotid was the seat of an annular endarteritis, which had diminished, but not entirely occluded the caliber of the vessel.

EMBOLISM OF THE CAROTID ARTERY. Embolic occlusion of the carotid in the neck appears to be even rarer than thrombosis. The only recorded cases are those of Cohn,¹⁹ Eichhorst,²⁰ and Haffner.²¹

¹³ Zwei Fälle von spontaner Allmählicher Verschleisung grosser Hals arterien Stamme, Deutsch. Klinik, 1872, No. 51.

¹⁴ Ueber Thrombose der Carotis, Deutsch. Arch. f. klin. Med., 1881, xxviii, 81.

¹⁵ Right Hemiplegia and Atrophy of the Left Optic Nerve, Proc. Royal Soc. Med., 1907-1908, i, 180.

¹⁶ Lehrbuch der Nerven Krankheiten, 1903, ii, 942.

¹⁷ Cited by Oppenheim.

¹⁸ L'Hemiplegie Progressive, Rev. Neur., 1898.

¹⁹ Klinik der Embolischen Gefäss Krankheiten, 1860, S. 364.

²⁰ Ueber Emboli der Carotis Communis, Med. Klinik., 1907, iii, 885.

²¹ Obliteration der Carotis Communis Sinistra in folge von Embolischer Arteritis bei Herzfehler, Deut. Arch. f. klin. Med., ix, 523.

In Haffner's case there had occurred an embolic occlusion of the left brachial artery in October, 1892. In 1895 there appeared suddenly parietal headache, vertigo, and visual disturbances; no paralysis. A painful swelling developed just below the left ear, and the left carotid and temporal artery were pulseless. Ophthalmoscopic examination was negative. Two years later, in March, 1897, there developed gradually, hemiplegia of the right side, which became complete in about a week. This was accompanied by some sensory loss as well. The patient became apathetic and later demented. Autopsy showed an organized thrombosis of the left carotid, which extended a little beyond the bifurcation. There were small foci of softening in the centrum semiovale on the left side.

HEMIPLEGIA ASSOCIATED WITH DIMINISHED PULSATION OF THE CAROTID ARTERY IN THE NECK. Under this heading I would call attention to the occurrence of diminished pulsation of the carotid artery in the neck on the side of the softening in cases presenting the symptoms of thrombotic hemiplegia.

Among a series of twenty cases of hemiplegia occurring in advanced life, which I examined for this symptom in the neurological service of the Montefiore Home for Chronic Invalids, it was possible to demonstrate its presence in four cases, all of which presented the clinical picture of an extensive lesion of the hemisphere: hemiplegia with contractures, hemi-sensory disturbances and mental deterioration. The optic nerves were normal on both sides in all four cases.

While inequality of pulsation on the two sides might be accidental, its occurrence in four cases all presenting the symptoms of extensive brain softening is rather significant, and the thought naturally arises that some obstructive lesion of the vessel or its entrance in the arch of the aorta has interfered with the free flow of blood to the brain, which in old subjects with weakened heart would be a predisposing factor in the production of senile softening of the brain.

Of course, further observations and pathological studies will be necessary in order to determine with certainty this point. If, however, these observations are confined, such a diminution in the pulsation of one of the carotids, would be a symptom of some prognostic value before the development of hemiplegia.

SOME CONCLUDING REMARKS. I would urge that all cases presenting cerebral symptoms of vascular origin, that the main arteries of the neck be carefully examined for a possible diminution or absence of pulsation. Obstructive lesions of these vessels are apparently rare, but it seems certain that cases are overlooked from failure to make clinical and pathological examinations from this point of view.

Probably in the large majority of cases, a sudden obstruction

may occur without softening, producing nothing more than mild, and transient cerebral symptoms. On the other hand, this may so cripple the cerebral circulation in advanced life, that functional deficiencies result and the one hemisphere may be more predisposed to softening processes than the other.

I would emphasize the occurrence of *diminished pulsation of the carotid on the side of the softening as an occasional symptom in cases of thrombotic hemiplegia*, and suggest that the impairment of circulation through the carotid so interferes with the general circulation of the hemisphere as to predispose to thrombus formation and encephalomalacia. A diminished pulsation from this point of view would merit a place as a prognostic factor of importance.

There are various clinical pictures resulting from obstruction of the carotid, similar in symptomatology to those accompanying the intracranial vascular degeneration and diseases. Among these are hemiplegia, chronic progressive hemiplegia, the chronic progressive softening of the brain (Wernicke), and optic atrophy with contralateral hemiplegia.

The distinguishing feature is an absence of the carotid pulse on the side corresponding to the lesion. Should the thrombosis extend to the bifurcation and include the external carotid, the temporal artery on the affected side will be pulseless.

I would also particularly emphasize the occurrence of *unilateral vascular changes, pallor, or atrophy of the disk with contralateral hemiplegia* in obstruction of the carotid artery.²²

It is also important to note, that the visual disturbances and vascular changes in the optic nerve may precede other organic cerebral symptoms, the collateral circulation failing to develop in the distribution of the ophthalmic artery.

Unilateral headaches and vertigo, especially in assuming the upright posture, epileptiform attacks, failing memory, attacks of threatened hemiplegia, cerebral intermittent claudication, are some of the vascular symptoms which should suggest the possibility of carotid obstruction.

In the realm of pathology, such conditions as chronic edema, indurative, atrophic, and softening processes of the brain, in which the main vessels of the circle of Willis are free from obstruction, should always give rise to the suspicion of impaired circulation in the carotid artery.

These various symptoms and syndromes and their underlying

²² This syndrome has also been described with intracranial vascular disease: Gowers (Embolism of the Middle Cerebral and of the Central Artery of the Retina, with Autopsy, *Lancet*, 1875, p. 794); Cadwallader (Unilateral Optic Atrophy and Contralateral Hemiplegia: Consequent on Occlusion of the Cerebral Vessels, *Jour. Amer. Med. Assoc.*, 1912, p. 2248); Guthrie and Batten (Unilateral Atrophy of the Optic Nerve Associated with Hemiplegia of the Opposite Side, *Trans. Chir. Soc.*, xxxvi, 52); Elsehung (Ueber die Embolie der Arteria Centralis Retina, *Arch. f. Augenheilk.*, 1891, xxiv, 65); and Starr (Diseases of the Nervous System, 1910, p. 500).

pathological conditions are all perfectly well-known, but as was remarked in the introduction to this paper, we instinctively associate them with intracranial vascular disease.

It may add to our knowledge of encephalomalacia and the accuracy of vascular localization if the main vessel in the neck is also considered.

A STUDY OF THE VALUE OF THE QUANTITATIVE ESTIMATION OF DISSOLVED ALBUMIN IN GASTRIC EXTRACTS (WOLFF-JUNGHANS' TEST) IN THE DIAGNOSIS OF GASTRIC CANCER.

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METHODS for the estimation of the soluble albuminous products of digestion have frequently been devised with the hope that such might prove of practical service in the differential diagnosis of gastric ailments. Of these methods, the well-known procedure advanced by Solomon had for a time the greatest vogue. Esbach's reagent and tubes proved, however, unsatisfactory and inaccurate from a clinical view-point. More recently the problem has been approached from the practical quantitative side and encouraging work recorded.

Wolff and Junghans¹ report a method for estimation of the amount of soluble albumin in gastric extracts which they claim have given excellent clinical information in Ewald's service at the Augusta Hospital, Berlin.

Theoretically, their procedure has the following basis: In the normal aspirated test-meal there is demonstrable relatively large quantities of soluble albumin by means of precipitating reagents. This soluble albumin appears only through the agency of the gastric enzymes. This fact is proved by testing for soluble albumin a similar test-meal which has been chymified but not swallowed. In such event, only minute quantities of dissolved albumin are present.

Acting on these observed facts, Wolff and Junghans fed similar meals to sets of individuals revealing malignant and benign achylas. Their work appeared to show that in the malignant achylas, aspirated test meals were rich in soluble albumin, while in benign achylas very little of the albumin could be demonstrated.

¹ Berl. klin. Woch., May 29, 1911, and March 18, 1912; Medizinische Klinik, March 24, 1912; Taschenbuch der Magen und Darm Krankheiten, 1912.

Three suppositions have been advanced to explain this increased volume of dissolved albumin in the malignant achylia. It has been suggested that the excess of albumin is due (a) to interference with albuminous resorption; (b) to a "cancer milk" rich in albumin which exudes from malignant growths, and (c) to a specific, peptid-splitting ferment from the neoplasm, capable of carrying protein digestion as far as the completely soluble albumin stage.

Clinically, the reaction was shown to be positive in 18 of a series of 20 gastric cancers and negative in 14 of a series of 15 cases of simple achylia in Ewald's service. Recently, Rolph² has reported positive tests in all of 7 cases where cancer was present in the stomach or secondarily involved that viscus. In 8 cases of benign achylia the test proved negative. Rolph states that gastric contents contaminated with blood beyond a dilution of 1 to 3000 may give the reaction and cautions against positive interpretation in instances where there is high combined acid present. In such event peptone is usually present. He claims that cancer of the cardia is not so likely to give positive reaction as is cancer in other parts of the stomach.

AUTHOR'S STUDY. In the last 3950 patients presenting themselves for test-meal examination of gastric function in the Mayo Clinic, there were 747 instances where gastric extracts showed achylia or were associated with conditions likely to be confused with malignancy. These gastric extracts were all tested for soluble albumin by the Wolff-Junghans' method. Records were kept of the association of the results of this test with other test-meal and clinical findings. When the tabulations were completed the diagnoses were entered on the history sheets. In 78.4 per cent. of cases it was possible to obtain check upon diagnoses by operation.

Selection of Material and Mode of Procedure. The day previous to the examination of his gastric extract the patient was given 1 ounce of castor oil at 4 P.M. This was followed at 6 P.M. by a motor test-meal consisting of mixed food. At 7 P.M. twenty raw, seedless raisins were given. Twelve hours later (7 A.M. the following morning) the patient was fed 60 grams of second-day bread and 200 c.c. of water. This secretory test-meal was removed from fifty to sixty minutes after administering. The specimen secured was thoroughly mixed, filtered through double hydrochloric-acid-washed papers, and tested for dissolved albumin within an hour of its being obtained from the stomach. On account of the fact that, as has been shown in this clinic,³ but 52.2 per cent. of cases of gastric cancer yield gastric extracts revealing absence of free hydrochloric acid, and that in 15.7 per cent. of cases, free hydro-

² Med. Record, New York, May 10, 1913, p. 849.

³ Smithies, *The Significance of Gastric Ulcer with Respect to Gastric Cancer*, Jour. Amer. Med. Assoc., November 15, 1913, p. 1793.

chloric acid ranges between 20 and 50 per cent., we have deemed it advisable to apply the test for soluble albumin not only to achylia, but also to gastric extracts where the free hydrochloric acid was below 20 per cent. In a few instances of suspected malignant ulcer we have performed the test upon gastric extracts with higher free hydrochloric acid content. In such we have been fully alive to the possibilities of error, but for the purpose of gaining information and for comparison we have deemed it wise to make the test.

Procedure. Six absolutely clean test-tubes are required for each test. Those of the narrow type and of 20 c.c. capacity answer very well. The tubes are numbered serially from 1 to 6. They receive respectively 1 c.c., 0.5 c.c., 0.25 c.c., 0.1 c.c., 0.05 c.c. and 0.025 c.c. of the filtered gastric extract. These amounts are readily measured by means of a 1 c.c. pipette, graduated in $1 - \frac{1}{100}$ c.c. By means of a 10 c.c. pipette, graduated into $1 - \frac{1}{10}$ c.c., the volume in each test-tube is next consecutively brought up to 10 c.c. volume with distilled water. This gives from the tubes 1 to 6 dilutions of gastric juice varying respectively from 1 to 10 to 1 to 400 (viz., 1 to 10, 1 to 20, 1 to 40, 1 to 100, 1 to 200, and 1 to 400). These figures we have termed "units" of precipitable albumin. The tubes are then inverted several times to insure complete mixture of their contents. One c.c. of the reagent to precipitate the albumin in solution is then carefully layered upon the contents of each tube. The precipitating reagent suggested by Wolff has proved satisfactory with us. It has the following formula:

Phosphotungstic acid (puriss).	3 c.c.
Hydrochloric acid (concentrated)	10 c.c.
Alcohol (96 per cent.)	200 c.c.
Aq. dest.	q. s. ad 2000 c.c.

Mix and keep in a glass or rubber-stoppered flask in a cool place.

Manifestation and Interpretation of the Test. If there has been dissolved albumin in any of the tubes, the juncture of the Wolff reagent with the diluted gastric extracts is marked by a pearly white zone or "ring." This is better brought out if the tubes are inspected against a black background. (We have used a piece of black cloth such as photographers employ when focussing cameras.) The tubes should be inspected at once after adding the Wolff solution. Prolonged standing allows cloudy zones to form which render comparative interpretation dubious.

We have interpreted our results after Wolff and Junghans' suggestion. If the white ring of precipitated albumin appears in tubes 1, 2, and 3 (namely, units of albumin from 10 up to 50) and no further manifestations are present in the remaining three tubes we have called the test negative. If tubes 1, 2, 3, and 4 exhibit rings (units of albumin from 10 to 100) we have considered the

reaction doubtful. The presence of white rings in tubes 1, 2, 3, 4, 5 and above (units of albumin ranging from 10 to 200 to 400) we have taken to denote a positive test.

Results. The gross results of our work are as follows: Of 747 gastric extracts of the class described above, 318 (42.6 per cent.) gave 200 to 400 units of precipitable albumin; 112 (15.7 per cent.) exhibited 100 units, and 317 (42.4 per cent.) showed less than 100 units. In this grouping, 71.5 per cent. of the gastric extracts were from cases showing some degree of gastric retention.

Consideration of Cancer Cases. There were 215 cases of operatively and pathologically demonstrated gastric carcinoma in this series. In 141 (65.1 per cent.) units of precipitable albumin ranged from 200 to 400. In 29 instances (13.4 per cent.) there were 100 units of albumin shown. Combining the returns it is evident that 170 (78.5 per cent.) of the proved cases of gastric cancer gave either undoubtedly positive or suspiciously positive Wolff-Junghans' test. In 45 cases (21 per cent.) the test was negative, less than 100 units of precipitable albumin being demonstrated. Of this group of 215 cases of gastric cancer, 73.2 per cent. exhibited some grade of motor stagnation.

Gastric extracts from 15 cases of *ulcus carcinomatosum* were tested. In 11 instances (73.3 per cent.) units of precipitable albumin ranged between 200 to 400. In 3 (20 per cent.), 100 units were shown. In other words, of the 15 cases of malignant gastric ulcer, 14 (93.3 per cent.) were either definitely positive or suspiciously so to the Wolff-Junghans' test. One case (6.6 per cent.) exhibited below 100 units of albumin. In this group, motor stagnation of some degree was present in 86.6 per cent.

Combining the results from the cases of frank gastric carcinoma and those of *ulcus carcinomatosum*, it is seen that of a total of 230 cases, 184 (80 per cent.) returned positive or suspicious Wolff-Junghans' test.

Relation of Manifestations of Test to Location of Malignant Process. We examined gastric extracts from 10 cases of cancer involving the cardia. Six cases (60 per cent.) gave positive test, 1 (10 per cent.) was suspicious, and 3 (30 per cent.) were negative. Thus 70 per cent. of our cases of cancer at the cardia showed units of precipitable albumin ranging from 100 to 400.

There were 5 cases of cancer of the fundus in our series; 1 (20 per cent.) was positive, 1 (20 per cent.) was doubtful, and 3 (60 per cent.) were negative.

We have records of 44 cases where the neoplasm involved mainly the lesser curvature of the stomach. Of this group, 33 cases (75 per cent.) gave clearly positive Wolff-Junghans' test, 4 (9.1 per cent.) were suspicious, and 7 (15.8 per cent.) were negative. It is evident that 84.1 per cent. of cancers involving the lesser curvature show units of precipitable albumin ranging from 100 upward.

In our series there were 3 cases of cancer of the greater curvature. Two cases (66.6 per cent.) were positive and the remaining case suspicious. Thus all showed 100 plus units of albumin.

Eight of our cases were proved to have cancer involving mainly the posterior wall of the stomach. Of this group but 3 cases (37.5 per cent.) were positive to the test, while 5 cases (62.5 per cent.) were negative.

The pars media was involved 14 times. Of this number, 11 cases (78.5 per cent.) gave positive test and 3 cases (21.5 per cent.) were negative.

In 93 instances the malignant growth was at the pylorus and antrum. In this class, 59 cases (63.4 per cent.) showed units of precipitable albumin from 200 upward, 8 cases (8.6 per cent.) were suspicious, revealing 100 units, and 25 cases (26.9 per cent.) were negative. In other words, 72 per cent. of the cancers at the pyloric region gave a positive or suspicious Wolff-Junghans' test.

Our series includes 38 cases where the stomach showed general or extensive malignant involvement. In 26 instances (68.5 per cent.) the test was positive, in 3 cases (7.9 per cent.) it was suspicious, while 9 times (23.6 per cent.) negative results were obtained.

Comparison of Other Test-meal Findings in the Cancer Cases with the Wolff-Junghans' Test. It might be profitable here to emphasize the diagnostic relation of other tests associated with that for dissolved albumin in the gastric extracts from our malignant cases. It will be noted above that of the 230 cancer and malignant ulcer cases the Wolff-Junghans' test was positive or suspicious in 184 (80 per cent.). In this same group of cases, free hydrochloric acid was absent in 52.2 per cent., lactic acid was demonstrated in 48.8 per cent., "occult" or altered blood shown in 75 per cent., glycytryptophan test present in 40 per cent. (141 cases), the average formal index (method of Sorenson and Schiff⁴) was 21 (57 cases), and organisms of the Boas-Oppler group were demonstrated in 93.8 per cent. (146 cases) by the colored agar method.⁵ Some degree of gastric retention was shown in nearly 74 per cent. of the entire group of cancer cases, irrespective of the location of the growth.

The Wolff-Junghans' Test in Extragastric Cancer: Liver and Gall Tract. Our series includes 15 instances of malignancy in this location. In 5 cases (33.3 per cent.) the test was positive, in 3 cases (20 per cent.) it was suspicious, and in 7 cases (46.6 per cent.) it was negative. Thus 8 cases (53.3 per cent.) of extragastric malignancy showed units of albumin from 100 upward. Some degree of motor stagnation was evidenced in 26.6 per cent. of these cases.

The *pancreas* was the seat of malignant processes three times.

⁴ Zeitschrift für physiologische Chemie, 1909, xiii, 27.

⁵ Smithies, Arch. Int. Med., June, 1911, p. 736.

In no instance was a positive Wolff-Junghans' test obtained. Motor defect was not noted in any of these cases.

There was 1 case of cancer of the *transverse colon*. It gave a negative test. There was normal gastric motility in this case.

Gastric Syphilis. We have tested gastric extracts for dissolved albumin from 5 cases. The reaction was positive in 2 instances (40 per cent.), suspicious in 1 (20 per cent.), and negative in 2 (40 per cent.). In one of the positive cases the specific process in the stomach was associated with multiple and exuberant ulceration. Gastric motility was interfered with in 1 case (20 per cent.) of this group.

Primary Anemias (mainly pernicious). Twenty-four cases of achylia in severe anemia comprised this class. In none of them was gastric stagnation present. Twenty-three (95.6 per cent.) of this group were negative to the Wolff-Junghans' test. In but 1 instance (3.3 per cent.) were the units of precipitable albumin above 200.

Simple Achylia Gastrica. We examined gastric extracts from 35 such cases. Gastric stagnation was proved in 4 cases (11.9 per cent.). In 22 instances (63 per cent.) of this type of achylia the test was negative, in 9 instances (25.9 per cent.) suspicious, and positive but 4 times (11.9 per cent.).

Achylorhydria. In addition to the cases of absent free hydrochloric acid mentioned in the above groups there were 212 cases of non-malignant disease showing achylorhydria. Gastric motility was impaired in 22 cases (10.3 per cent.). In this group 136 cases (64.1 per cent.) were Wolff-Junghans negative, 41 cases (19.3 per cent.) were doubtful, and 35 cases (16.5 per cent.) were positive.

Simple Gastric Ulcer. A number of cases of this affection and of duodenal ulcer were studied for purposes of comparison with the malignant cases. Their gastric extracts generally showed low free hydrochloric acid content. We tested extracts from 33 cases of operatively demonstrated gastric ulcer for dissolved albumin. In 16 instances (48.4 per cent.) units of albumin ranged above 200, in 6 instances (18.1 per cent.) the units ran as high as 100, while in 11 cases (30.3 per cent.) units of albumin were below 100. It is thus apparent that 66.5 per cent. of the proved cases of simple gastric ulcer were positive or suspicious to the Wolff-Junghans' test. Gastric motility was delayed in 39.4 per cent. of this group.

Duodenal Ulcer. Gastric extracts from 18 cases of duodenal ulcer were tested. In 12 cases (66.6 per cent.) units of albumin ranged above 200, in 2 cases (11 per cent.) at least 100 units were present, while 4 times (22.7 per cent.) less than 100 units were demonstrated. It is thus evident that 78 per cent. of our cases of duodenal ulcer were Wolff-Junghans' positive or suspicious. In this group, gastric stagnation was present in 55.5 per cent. of the cases.

Nephritis and Cardiovascular Disease. Our series include 12 cases of cardiorenal affections associated with obscure gastric complaint and anemia. The gastric extracts showed achylia. In 6 instances (50 per cent.) the Wolff-Junghans' test was doubtful, while in an equal number it was negative. The doubtful cases were associated with some degree of gastric motor insufficiency.

Cases Exhibiting Low Gastric Acidity. In this group we include 159 instances where gastric acidity ranged from 2 to 70. The average was 18.7. This group furnished what might be regarded as controls on our reactions in other groups, as well as demonstrated what results might be expected from the Wolff-Junghans' test in extragastric, malignant, and non-malignant ailments. It should be emphasized that all of the patients examined complained of some gastric disturbance. The finding of the low free hydrochloric acid in some instances might have led to suspicions of malignancy by those who hold gastric acidity as a strong index of such condition. This might have been especially so when we recall that the average age of our patients is above forty years.

Clinically, this group was varied as to diagnosis. Among the affections were appendicitis, cholecystitis, cholelithiasis, alcoholic gastritis, gastric neuroses, pulmonary tuberculosis, tabes, multiple sclerosis, tuberculous peritonitis, nephrolithiasis, pancreatitis, cirrhosis of the liver, pregnancy, malaria, diabetes, aneurysm of the abdominal aorta, chronic constipation, hemophilia, cancer of the breast, cancer of the lip, etc.

Of this heterogeneous group of low gastric acidity cases, 40 (25.1 per cent.) were Wolff-Junghans' positive, 38 (23.9 per cent.) were doubtful, and 81 (50.9 per cent.) were negative. In other words, of this class nearly 50 per cent. of cases showed units of precipitable albumin from 100 upward. Gastric motility was interfered with in some degree in 25 cases (15.7 per cent.).

Relation of the Wolff-Junghans' Test to the Presence of Blood in Gastric Extracts. We have frequently tested gastric contents that were discolored bright red by traumatic blood without getting positive Wolff-Junghans' tests. Of our entire series of 747 cases herewith detailed, "occult" blood was demonstrated by the benzidin test in 43.2 per cent. Reference to the gross summary of our work above will reveal the fact that we obtained positive tests for precipitable albumin in 42.6 per cent. of the gastric extracts of the entire series, while in 15 per cent. the test was doubtful. There may be more than a curious relationship between these groups of figures.

SUMMARY. The work herewith submitted appears to justify the following conclusions:

1. When carefully performed and interpreted the Wolff-Junghans' test for demonstration of dissolved albumin in gastric extracts was positive or suspicious in 80 per cent. of our series of gastric

cancer. In this series it was a more constant finding in gastric extracts than were absent free hydrochloric acid, the presence of lactic acid, and the glycyltryptophan test. It was rather more constant than tests for occult blood and the demonstration of gastric motor inefficiency. It was not so consistent in its manifestation as the demonstration of organisms of the Boas-Oppler group or the increase in the formol index.

2. In extragastric malignancy, gastric syphilis, and nephritis the Wolff-Junghans' test is inconstant.

3. In the differentiation between malignant and non-malignant achylas the Wolff-Junghans' test, when interpreted in connection with other clinical and laboratory data, is of considerable value. Positive reactions are rarely obtained in the achylas of primary anemia, simple achylia gastrica, and simple achlorhydrias when such are unassociated with gastric motor inefficiency.

4. Simple gastric and duodenal ulcers, especially when accompanied by pyloric stenosis or gastric atony, may give confusing responses to the Wolff-Junghans' test.

5. The presence of blood in gastric extracts may be a factor in the production of certain atypical positive tests.

JAUNDICE IN TUBERCULOSIS.

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JAUNDICE is caused by the presence of bile pigment in the blood. It is now acknowledged that the passage of the bile pigment is by way of the lymphatics into the thoracic duct and thus into the general circulation, and is always caused by some obstruction, whether extrahepatic or intrahepatic, to the normal flow of the bile. Rolleston divides jaundice into: "(1) Extrahepatic or 'obstructive' where there is a gross obstruction, usually involving the larger extrahepatic bile ducts, to the flow of bile along the bile ducts. (2) Toxemic, intrahepatic, or hemohepatogenous, where there is obstruction in the small intrahepatic bile ducts. The obstruction is due to cholangitis or inflammation of the minute ducts, depending upon the irritating effect of poisons derived from the blood circulating through the liver." In tuberculosis we find jaundice caused by both extrahepatic and intrahepatic obstruction to the flow of bile.

The extrahepatic cases have been caused by tuberculous glands in the portal fissure pressing upon the bile ducts. This is a rare condition, from the fact that the glands in the portal fissure receive the efferent lymphatic vessels conveying the lymph away from the liver and not those conveying lymph from the intestines and peritoneum. These glands become infected through the liver, which has become previously tuberculous from material brought by means of the portal vein from tuberculous intestines and peritoneum. Florand reported a case that had been jaundiced for two months. A diagnosis of obstruction of the gall duct by a calculus or neoplasm was made. Operation was performed, but the patient died of hemorrhage from the portal vein, due to injury in trying to remove a bunch of tuberculous glands that extended from the duodenum to the portal fissure of the liver. Hodenpyl reported a case of a colored man who had jaundice which the autopsy showed was caused by occlusion of the common duct by a mass of tuberculous lymph glands. Knight reported a case of a child, aged six years, who had increasing jaundice up to the day of death. The autopsy here also showed a mass of tuberculous lymph glands the size of a walnut in the transverse fissure of the liver and around the hepatic duct and portal veins. Köster reported a case of a three-year-old boy who had been jaundiced for two years. A little while before death the jaundice disappeared. At the autopsy there was found in the portal fissure a tuberculous gland that had become caseous and opened into the common bile duct.

The intrahepatic, toxemic, or hemohepatogenous cases of jaundice occur in those cases where there is tuberculosis of the liver itself. Tuberculosis of the the liver may manifest itself in three ways: (1) miliary tubercles, (2) solitary tubercles, and (3) tuberculous cirrhosis. It is only in the first two forms of tuberculosis of the liver that any cases of jaundice have been reported.

Miliary tubercles of the liver are of frequent occurrence. Arnold considered them almost a constant finding in cases of tuberculosis. Rosenberger found miliary tubercles in 83.8 per cent. of livers examined histologically. Simmond found them in 76 per cent. in adults, in 92 per cent. in children, and in 82 per cent. in general. Ullom in examining histologically 100 livers found miliary tubercles in 79. Rolleston puts the occurrence of miliary hepatic tubercles in fatal cases of ordinary pulmonary tuberculosis lower than 50 per cent. Miliary tubercles are found in the liver in cases of general miliary tuberculosis; in these cases the infection is carried by the hepatic artery; or they are found in cases of tuberculosis of the intestines and peritoneum, and in these cases the infection is carried by the portal vein. Ullom in the histological examination of 79 livers containing miliary tubercles found the position of the tubercles to be periportal 40 times, intra-acinal 17 times, and both periportal and intra-acinal 22 times. In 45 cases, examined

especially to see the relationship between intestinal ulceration and miliary tuberculosis of the liver, 38 cases showed intestinal ulceration. In these 38 cases the tubercles were found periportal 26 times, intra-acinal 3 times, and both periportal and intra-acinal 9 times.

Although miliary tuberculosis of the liver is such a common finding in tuberculous cases, jaundice caused by it is rare. Rolleston states it to be so rare that it is a curiosity. In 570 autopsies performed upon patients dying of chronic pulmonary tuberculosis at the Henry Phipps Institute, there has been only 1 case of jaundice caused by miliary tuberculosis of the liver.

CASE 2252.—A white man, single, aged twenty years, was admitted to the wards on March 31, 1904. Both he and his father had been hard drinkers, and his father had died of phthisis three years before. He had been sick for six weeks before admission, having been treated at another hospital for typhoid fever. He complained of slight cough, moderate expectoration of a greenish-yellow color, constipation, and night sweats. Examination showed advanced disease of both lungs. The heart had a diffuse pulsation over the whole precordium. The second pulmonic was accentuated. No murmurs were heard, and the dulness was normal. The liver extended two finger breadths below the costal margin. The spleen was palpable one and a half finger breadths below the costal margin. The abdomen was distended. On May 5, the patient was slightly jaundiced, not pronounced, simply an icteroid hue. There was marked tenderness over the liver. By May 14 the icteroid hue was less marked. The patient died on June 24.

The autopsy showed tuberculosis of the lungs, with cavity formation, miliary tubercles, edema, pneumonia, and bronchiectasis; parenchymatous nephritis; enlarged mesenteric glands; small ulcer in the appendix; adhesive pleurisy; fatty liver; heart slightly enlarged, valves normal. The liver was enlarged, weighing, 1860 grams. It was of firm consistence, dark red in color, and had rounded edges. Microscopic examination showed a marked grade of congestion, with distention of the capillaries and characteristic miliary tubercles, with large giant cells, epithelioid and round cells, and caseation.

The other type of tuberculosis of the liver in which jaundice manifests itself is the solitary tubercle, which is classified in three ways: (1) conglomerate tubercle, (2) tuberculous cavities or bile duct tuberculosis, and (3) tuberculous abscess. Conglomerate tubercles are comparatively large caseous masses found in the liver. W. Hale White, discussing this condition, says that before these caseating masses break down they may, unless care is taken, be mistaken for nodules of lymphadenoma. These conglomerate tubercles undergo caseation, soften, and at times, when situated

near the bile ducts, rupture into them leaving small cavities in the liver. Solitary tubercles, in whatever form they appear, are an extremely rare type of tuberculosis of the liver. The writer has been unable to find in the literature a single case of conglomerate tubercles of the liver that showed jaundice. However, two such cases have occurred at the Phipps Institute.

CASE 2662.—A white woman, aged forty years, was admitted to the wards of the Phipps Institute August 8, 1904. Her father died at the age of forty-five years of tuberculosis. Mother died at the age of thirty years in confinement. She had one brother and one sister living and well. Two sisters died young of some unknown cause. She had never been sick, but gave a history of excessive use of alcohol over a long period. In the last two years she had lost sixty pounds, and for the past six months had had a cough, worse at night, accompanied by a profuse yellow expectoration. She complained of pain in the lower anterior part of her right chest; dyspnea on exertion, attacks of hoarseness, lasting several days at a time; poor appetite; epigastric pain; distress after eating; constipation; passing blood in the stools; night sweats; slight edema of the ankles. Examination on admission showed an emaciated body, with a face of fairly good color. The heart was normal as well as the abdomen. The lungs showed infiltration of the upper part of the right upper lobe; consolidation, with some softening of the left upper lobe. On August 25 the liver was found slightly enlarged, edges hard, but smooth and not tender. On September 21 the patient was markedly jaundiced; the liver was slightly enlarged. Pressure in the epigastrium caused a great deal of pain. No mass could be felt. On September 26 blood examination showed erythrocytes, 3,840,000; leukocytes, 10,000. The blood was pale and coagulated slowly. The jaundice had become more marked. The conjunctivæ were of a bright yellow color. The whole body was now deeply jaundiced, and pain in the epigastric region was more marked. The liver was distinctly palpable, and the edges sharp and hard. The enlargement was more apparent in the left lobe. On October 1 the jaundice was intense, the abdomen flabby, and distended. There was some free fluid in the peritoneal cavity. Several purpuric spots appeared on the abdomen. From this time on the patient rapidly grew weaker, the jaundice being extreme, pain marked in the epigastrium, sordes on teeth and tongue, pulse weak and irregular, and she finally died on October 7. The temperature varied between 98° and 101° to 103° until fifteen days before death, when it dropped below normal and so remained until the end. The pulse was between 100 and 120 to 130, and respiration ranged from 27 to 40. The autopsy on October 8 showed ulcerated tuberculosis of the left lung, tuberculous pneumonia and edema of the right lung, miliary tuberculosis of the spleen, fatty infiltration of the heart,

fatty kidneys, with tubercles. The peritoneum contained about 1000 c.c. of yellow, slightly turbid fluid. The liver was enlarged and weighed 2016 grams; dense and granular on the surface; edges were rounded; its color was pale; scattered throughout were numerous small yellowish-white areas of firm consistence, some few were coalesced. The bile duct was patulous. The gall-bladder was distended with fluid, glycerin-like in consistency. Microscopic appearance: Many caseous areas, containing no giant cells and surrounded by epithelioid and small round cells; there were also typical miliary tubercles containing giant cells. The caseous nodules corresponded to the yellowish-white nodules seen macroscopically, and they contained tubercle bacilli in their periphery. There was an increase in the amount of fibrous tissue.

CASE 9808.—A white woman, single, aged forty-five years, was admitted to the wards of the Henry Phipps Institute August 19, 1911. Her father died at the age of sixty years of heart disease and her mother at the age of forty-five years, of dropsy. Four sisters died in childhood of unknown causes. She had two brothers living and well. In 1908 she had had an attack of typhoid fever, but otherwise her health had been good. She had lost about thirty pounds in the past four or five years, and for the past year had had a cough, worse at night, which was accompanied with profuse yellowish sputum. For the past year she had been dyspneic. Her appetite for some months had been poor, and occasionally she vomited. There had been constipation for the past eight months. She had had night sweats nearly every night for the past year. Examination showed advanced disease of both lungs and the outline of cardiac dulness enlarged. The liver was enlarged and extended below the costal margin. On January 23, 1912, there was noticed jaundice in the conjunctivæ. The jaundice increased, and in two days was marked over the whole body. The liver was markedly enlarged, reaching to the umbilicus. It was quite tender. The stools were loose and of a natural color. The patient was nervous and not clear mentally. She did not answer questions intelligently. The jaundice lessened a little until January 29, when it became a little more intense and then gradually decreased until February 10, the day before her death, when it became markedly increased. All this time the patient had a slight talkative delirium, with some delusions. The liver remained enlarged and tender, and at no time was bile found in the urine or feces. The temperature varied between 95° and 103° , the pulse between 90 and 120, and the respiration between 18 and 36.

The autopsy showed chronic pulmonary tuberculosis, chronic adhesive pleurisy, chronic tuberculous laryngitis, chronic pericarditis, with effusion, tuberculous enteritis and colitis, congenital cystic kidneys, and congestion of the spleen. The liver was enlarged, weighing 2300 grams. It was yellowish-brown in color, firm in

consistency, and had well-marked, rather sharp edges. On section it was yellowish-brown in color, and there were seen numerous small yellow areas, fairly well-outlined, about 1.5 to 2 cm. in diameter, arranged in groups of four or five. Scattered in many places, closer and more numerous, were smaller areas about 1 mm. in diameter. They were poorly defined, raised above the surface, translucent, and gray. In many places the interlobular septum was thickened. Iodine test for amyloid was positive. The gall duct was patulous. The gall-bladder was normal in size, and contained a dirty reddish-brown, thick fluid.

Rolleston in discussing bile-duct tuberculosis states it is remarkable that jaundice is constantly absent, inasmuch as there is definite obstruction in at any rate some of the bile ducts. Bristowe found 12 cases of small tuberculous cavities of the liver in 167 cases of tuberculous ulceration of the intestines, but he makes no statement whether or not jaundice was present in any of them. Thayer has reported a case of tuberculous cavities of the liver which showed jaundice for a week, but cleared up some time before death. Warthin had a case of bile-duct tuberculosis which had intense jaundice for three months before death.

At times the solitary tubercles become secondarily infected with pyogenic microorganisms, soften down, and form abscesses. Mayo-Robson has reported a case of tuberculous abscess of the liver which was successfully operated on and made a complete recovery. He states that for three months prior to the operation the patient had a slight tendency to jaundice.

That jaundice is a rare condition in tuberculosis is admitted by almost all who have had any experience in tuberculosis. Warthin has had a most unusual experience. He states that 80 per cent. of his cases of acute general miliary tuberculosis of the typhoid form have shown a well-defined icterus, either slight, moderate, or well-marked in grade, and about the same percentage of cases of chronic tuberculosis ending in a general miliary metastasis have also shown the same occurrence of jaundice. The writer's experience at the Phipps Institute dealing with chronic pulmonary tuberculosis for the most part had been quite different. In 570 cases that have come to autopsy in that institution, there has been but 3 cases of icterus; the findings in these cases are reported above. In addition to these 3 cases that died in the institute there were 4 other cases (Nos, 379, 1155, 3495 and 4748) that have shown jaundice; 3 of them showed a slight grade of jaundice and 1 a distinct icterus. These 4 cases left the hospital before death, and, of course, we could not prove that the jaundice was due to a tuberculous condition of the liver. These 7 cases of jaundice are all that have occurred in 1748 cases that have been in the wards of the hospital from the time of its inception until February 1, 1912.

From such a small number of cases it is impossible to draw

any conclusions, but taken in connection with cases reported in the literature they are suggestive: (1) Jaundice occurring in the course of chronic tuberculosis is probably due to some form of tuberculosis of the liver, either extrahepatic or intrahepatic. (2) The grade of the jaundice is helpful in surmising the pathological condition, intense jaundice being probably due either to pressure of tuberculous glands on the extrahepatic ducts or to some form of the solitary tubercles of the liver; milder forms being produced by a miliary tuberculosis of the liver.

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HYALINE DEGENERATION OF THE ISLANDS OF LANGERHANS IN NON-DIABETIC CONDITIONS.

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HYALINE degeneration of the islands of Langerhans was first described in 1900 by Opie,¹ who noted its association with diabetes mellitus. Since then numerous observers have encountered hyaline islands in diabetes, and the condition is now recognized as a common finding in this disease.

In a series of 90 cases of diabetes which I² studied in 1909, sclerosis of the islands was noted in 60, and hyaline degeneration

¹ *Jour. Exp. Med.*, 1900 to 1901, v, 397, 527.

² Cecil, *Jour. Exp. Med.*, 1909, 266; 1911, xiv, 500.

in 30 per cent. of the cases. Although hyaline change in the islands is so frequently encountered in the diabetic pancreas, its occurrence in the non-diabetic pancreas is rare—so rare, indeed, that the lesion is generally considered characteristic of diabetes. I have been able to find only five references to such exceptional cases in the literature.

The first case of hyaline degeneration of the islands without diabetes was reported by Ohlmacher³ in 1904. The case was that of an man, aged seventy-two years, the immediate cause of whose death was mastoiditis, with thrombosis of the lateral sinus. At autopsy there was cirrhosis of the liver, chronic interstitial pancreatitis, arteriosclerotic atrophy of the kidneys, and general arteriosclerosis.

Fully four-fifths of the islands of Langerhans showed hyaline degeneration, while many of the surviving ones were hypertrophied. This patient had been under observation for nine months previous to his death, and at no time had he shown any symptoms of diabetes.

Whipple,⁴ in 1907, in a study of pancreatitis and focal necroses, refers very briefly to two cases of hyaline degeneration of the islands that he observed in which there had been no evidence of diabetes. The first case was a colored man, aged twenty-three years, who died of tetanus. The anatomical diagnosis was appendectomy, general peritonitis, lobar pneumonia, focal necroses of the liver, cardiac hypertrophy, chronic gastritis, and chronic interstitial pancreatitis. The pancreas showed in addition to chronic inflammatory changes, hyaline degeneration of the islands of Langerhans.

Through the kindness of Dr. Whipple, I have been able to include the second of his cases in the present series. It will be described in detail farther on.

Saltykow,⁵ in 1909, noted well-marked hyaline degeneration of some of the islands in the pancreas of a man, aged eighty-eight years, with advanced arteriosclerosis. There were also a number of necrotic foci in the pancreas (fat necroses?). At no time had he shown symptoms of diabetes.

Herxheimer⁶ refers to a case of cirrhosis of the liver in which the pancreas was sclerotic and showed in addition a number of hyaline islands. At the time of the patient's death there was no diabetes, but on looking up his past history it was found that diabetes had existed before the onset of cirrhosis of the liver.

Milne and Peters,⁷ in 1912, remarked that they had encountered

³ AMER. JOUR. MED. SCI., 1904, cxxviii, 287.

⁴ Bull. Johns Hopkins Hospital, 1907, xviii, 391.

⁵ Korrespondenzbl. f. Schweiz Aerzte, 1909, xxxix, 625.

⁶ Verhändl. d. deutsch. path. Gesellsch., 1909, p. 276.

⁷ Jour. Med. Research, 1912, xxvi, 405.

hyaline degeneration of the islands in non-diabetic conditions, but beyond that statement proceeded no further in the matter.

Of the 6 cases reported in this paper, 4 came from the clinics of the Presbyterian Hospital, 1 from the pathological department of the New York Hospital, and 1 from the pathological department of the Johns Hopkins Hospital. Synopses of these cases will be found at the end of the paper. A comparative study of these cases might be profitable as a means of approaching the problems of the pathogenesis of diabetes, particularly as regards the part played by the islands of Langerhans. In order to facilitate this comparison, I have prepared a table in which are catalogued the more important clinical and pathological data from the six cases.

TABLE OF CASES.

Case.	Age.	Sex.	Cause of death.	Pancreas.	Liver.	Kidneys.	Cardiovascular system.
I L. M.	60	M.	Epithelioma of inferior maxilla.	Chronic interstitial pancreatitis. Many fibrous and hyaline islands. Arterioles thickened.	Moderate cirrhosis.	Fibrous and hyaline glomeruli. Arterioles thickened and hyaline.	General arteriosclerosis. Chronic interstitial myocarditis.
II C. H. B.	43	M.	Cirrhosis of liver.	Slight chronic interstitial pancreatitis. Fibrous and hyaline islands. Arterioles thickened.	Advanced cirrhosis.	Fibrous and hyaline glomeruli. Arterioles slightly thickened.	General arteriosclerosis. Chronic endocarditis.
III M. M.	50	F.	Acute pericarditis.	Fat necroses. Moderate interstitial sclerosis and adiposis. Many hyaline islands. Arterioles thickened.	Fatty infiltration.	Chronic interstitial nephritis. Fibrous and hyaline glomeruli. Arterioles thickened.	General arteriosclerosis. Chronic endocarditis. Chronic myocarditis. Cardiac hypertrophy.
IV F. W.	42	M.	Typhoid fever.	Some sclerosis. Considerable adiposis. Many hyaline islands, a few hypertrophied. Arterioles thickened.	Focal necroses. Cloudy swelling.	Numerous hyaline glomeruli. Cloudy swelling. Arterioles thickened.	Arteriosclerosis.
V D. H.	37	M.	Endothelioma (?) (left orbit).	Metastases. Slight sclerosis. Many islands hyaline; some hypertrophied. Arterioles slightly thickened.	Metastatic nodules.	A few hyaline glomeruli. Compression atrophy about metastases. Glomerular capillaries thickened.	Slight atheroma of aorta.
VI H. T.	49	F.	Cardio-renal disease.	Considerable interstitial sclerosis. Many hyaline islands. Arterioles thickened.	Congestion.	Chronic diffuse nephritis. Many fibrous and hyaline glomeruli. Arterioles thickened.	Cardiac hypertrophy and dilatation. Diffuse myocarditis and fatty degeneration. Verrucous endocarditis. Arteriosclerosis.

In the first place it will be noticed that the condition occurred in middle-aged or elderly people, in this respect resembling diabetes. Four of the six cases were in men. None of the cases gave any history of diabetes; in none of them did the urine show glucose while under observation; in none of the cases was there any his-

tory or evidence of lues; in three there was a history of excessive indulgence in alcohol.

The immediate cause of death was an acute infection in 2 cases, a malignant neoplasm in 2, chronic nephritis in 1, and cirrhosis of the liver in 1 case.

The most interesting points from comparison bore on the pathological changes noted in the various organs. In the first place there was noted in every case an interstitial pancreatitis of the type usually seen in diabetes, and more or less thickening of the pancreatic arterioles. The new-formed connective tissue was irregularly distributed, the pancreas appearing normal in some places, while in others there was definite interacinar sclerosis. In Cases IV and V the sclerosis was slight and visible at only a few points. The islands were in no instance entirely destroyed; on the contrary, perfectly normal islands could always be found. A certain number, however, showed more or less extensive hyaline degeneration, which apparently originated about the thickened insular capillaries. The hyaline changes were associated in most instances with a certain amount of insular sclerosis. So far as the pancreas was concerned then it would have been impossible to distinguish the lesions from those observed so frequently in diabetes.

In two of my cases there was a well-marked cirrhosis of the liver, a condition which also occurred in the cases of Ohlmacher and of Herxheimer. In Herxheimer's case there had previously been some glycosuria, but at the time of the hepatic cirrhosis the glycosuria had entirely disappeared. Herxheimer suggested that the disappearance of the glucose might have been dependent in some way on the development of the hepatic cirrhosis.

The condition of the kidneys in my series is particularly interesting. In every case there was a definite fibrosis and hyaline degeneration of some of the glomeruli, associated with sclerosis of the renal arterioles and glomerular capillaries. The lesions were not advanced (except in two of the cases) and were confined for the most part to the glomeruli. The frequent association of chronic nephritis with diabetes has been often observed, especially in those cases where arteriosclerosis is present. Indeed, it is the arteriosclerotic type of nephritis that is usually seen in this connection.

In view then of the frequent association of diabetes and arteriosclerosis it is significant that in the present six cases of pancreatic and insular lesions, arteriosclerosis was noted in all; in four instances being associated with cardiac lesions. In Cases IV and V, the vascular changes were slight and largely confined to the smaller vessels of the pancreas and kidney, while in the remaining cases the process was more generally distributed.

DISCUSSION. What bearing has the occurrence of hyaline degeneration of the islands of Langerhans in non-diabetic conditions on the island theory of diabetes? For my own part I cannot see

that it vitiates that theory in any way. Certainly, no one would think of doubting the effect of sclerosis and hyaline degeneration of the glomeruli on renal efficiency, because one sometimes sees hyaline glomeruli in a kidney which during life has manifested no signs of disease.

Two explanations are open to us. In the first place it is quite possible that the destructive process in the islands has not advanced far enough to produce diabetes. The number of islands varies greatly in different individuals. Those with a large number could probably stand considerable destruction of island tissue without showing symptoms, for Nature has doubtless provided many more islands than are actually needed for efficient carbohydrate metabolism. Organs are constantly being encountered at the post-mortem which, while diseased, had not advanced as yet to the symptom-producing stage; for example, cirrhosis of the liver without jaundice or ascites, shrunken kidneys without albuminuria, endocarditis without incompetence, etc. So it may be assumed that destruction of the islands must progress to a certain point before glycosuria appears.

The other explanation is that the patient had diabetes at one time, but that other organs have vicariously assumed the pancreatic function with so much success that they have completely supplied the deficiency in that organ. Personally, I should rather favor the former hypothesis for the reason that in no one of the six cases had the hyaline degeneration involved all the islands. Moreover, one would expect to see more evidence of regeneration or hypertrophy of the islands if at any time there had been much demand for an increase in their functional activity. In a previous paper I⁸ have shown that in a considerable proportion of diabetic pancreases there has occurred more or less regeneration and hypertrophy of the islands, the new-formed islands budding off from the ducts after the manner of those observed in the fetal pancreas. The absence of this phenomenon may be taken to suggest that in the six cases which have been reported diabetes had at no time existed.

An interesting phenomenon observed in this study is the coincidence of hyaline degeneration of the islands and of the glomeruli. In the kidney, fibrous and hyaline glomeruli are very common, and have usually been interpreted as the sequel of renal arteriosclerosis. Possibly the same explanation holds for hyaline changes in the islands of Langerhans. It is conceivable that in both instances the vascular changes have involved particularly the capillaries supplying these structures, with the result that sclerosis and hyaline degeneration have ensued. And just as arteriosclerosis is now recognized as the usual precursor of the so-called "contracted kidney,"

with its interstitial fibrosis and glomerular lesions, so pancreatic diabetes may eventually be shown to depend upon a preëxistent arteriosclerosis, which, interfering with the pancreatic vascular supply has induced an interstitial pancreatitis and degenerative changes in the islands of Langerhans. I would also put forward the suggestion that the hyperglycemia which has been observed in cases of arteriosclerosis, with high tension, might be explained by the same theory as an incipient disturbance of the internal secretion of the pancreas due to pancreatic arteriosclerosis.

SUMMARY. Six cases of hyaline degeneration of the islands of Langerhans, in which there was no evidence of diabetes have been reported. All occurred in subjects aged over thirty-seven years. In addition to the hyaline changes there were found in every case more or less sclerosis of the insular capillaries, and a chronic interacinar pancreatitis of the type usually encountered in diabetes mellitus.

The explanation of this phenomenon, which has seemed most likely is that hyaline degeneration of the islands, may occur up to a certain point without producing diabetes. When a number of islands, sufficient to interfere with carbohydrate metabolism, have been involved, diabetes ensues.

The hyaline changes in the islands of Langerhans have been associated in every case with hyaline degeneration of the renal glomeruli. The lesions in both instances are possibly referable to sclerosis of the smaller vessels supplying these structures.

SYNOPSIS OF CASES.

CASE I.—L. M., male, aged sixty years. Admitted to Dr. Blake's service at the Presbyterian Hospital with epithelioma of lower jaw. Urine free from glucose. Patient died following partial resection of lower jaw.

Autopsy 8081. Anatomical diagnosis: Amputation of the left inferior maxilla (epithelioma), acute bronchopneumonia, general arteriosclerosis, chronic interstitial myocarditis, cirrhosis of the liver, cholelithiasis, chronic interstitial pancreatitis, chronic diffuse nephritis.

Pancreas: Small and firm. On section it contained considerable fatty tissue. Microscopically there was an irregularly distributed sclerosis and fatty infiltration. Arteries were thickened and hyaline. The epithelium lining the larger ducts had undergone adenomatous proliferation. Islands were numerous, some appearing normal, others sclerotic, still others, perhaps 25 per cent., showed more or less hyaline degeneration.

Liver: Weight, 1210 gm. Surface smooth, but on section, lobules were small and distinct. Microscopically there was considerable

increase of the interlobular connective tissue and infiltration of lymphoid cells. Hepatic arteries were thickened and hyaline.

Gall-bladder: Contained a large stone.

Kidneys: Weight (together) 290 gm. Macroscopically they showed nothing of interest. Microscopically the glomeruli showed fibrous and hyaline changes. There was considerable granular degeneration and disintegration of the tubular epithelium. Arterioles were thickened and hyaline. The thyroid and suprarenals were normal.

CASE II.—C. H. B., male, aged forty-three years; moderately alcoholic. Admitted to the medical service of the Presbyterian Hospital, with jaundice and continuous fever. After several weeks of observation he was transferred to the surgical side for exploratory laparotomy. At operation, cirrhosis of liver and ascites were found. Patient died several days after the operation. Repeated examinations of the urine were negative.

Autopsy 7781. Anatomical diagnosis: Cirrhosis of the liver, chronic endocarditis, chronic glomerular nephritis, chronic interstitial pancreatitis, general arteriosclerosis, chronic interstitial splenitis, acute bronchopneumonia.

Pancreas: In the gross was apparently normal. Microscopically there were patches of sclerosis here and there. Small arteries were thickened and hyaline. Islands were sclerotic and in many cases hyaline. The stroma was infiltrated with lymphoid cells in places. Ducts were normal.

Liver: Weight, 1440 gm. Surface was markedly granular. On section the organ was tough and the cut surface was granular, the yellow elevated lobules being separated by pale gray tissue. Microscopically there was typical cirrhosis in the advanced stage, with extensive new formation of small ducts and dense infiltration of stroma, with lymphoid cells. Hepatic arteries thickened and hyaline. Portal capillaries were dilated.

Kidney: Some of the glomeruli had been converted into hyaline or fibrous tufts. There was slight thickening of some of the vessels. Tubular epithelium was broken down in places.

CASE III.—M. M., female, aged fifty years. Admitted to the second medical service of the Presbyterian Hospital during an exacerbation of arthritis deformans. Urine showed faint trace of albumin and casts, but no glucose at any time during her stay of one year in the hospital. The patient died of acute pericarditis.

Autopsy 7981. Anatomical diagnosis: Acute serofibrinous pericarditis, chronic endocarditis (mitral and aortic valves), hypertrophy of heart, chronic interstitial myocarditis, chronic interstitial nephritis, fatty infiltration of the liver, chronic interstitial pancreatitis, fat necroses in the pancreas, general arteriosclerosis, hypertrophic arthritis deformans, etc.

Pancreas: Firm and of good size. Small yellowish areas scattered

over the surface. Islands visible. Ducts normal. Microscopically there was some increase of the stroma in places and considerable adipose tissue was found between the lobules. Here and there were collections of lymphoid cells, and at some points in the fatty tissue there were seen small foci of necrosis, surrounded by leukocytes. The islands were numerous and rather large. About two-thirds of them showed definite hyaline changes, the process being advanced in some cases. Small arteries were thickened and hyaline.

Liver: Centres of lobules congested. Hepatic arteries showed considerable thickening and hyaline degeneration.

Kidney: Well-marked increase of stroma in the cortex, especially about the glomeruli; the latter showed fibrous and hyaline changes, moderate infiltration of stroma, with lymphoid cells. Small arteries were thickened and hyaline. The cells of the convoluted tubules were in places granular and vacuolated.

Thyroid: Slight increase of stroma. Suprarenals and hypophysis were normal.

CASE IV.—F. W., male, aged forty-two years. Admitted to the second medical service at the Presbyterian Hospital for typhoid fever. Died ten days after admission, with bronchopneumonia. Urine was negative.

Autopsy 8197. Anatomical diagnosis: Typhoid fever, typhoid ulcers of the ileum and ascending colon, acute splenic tumor, focal necroses of the liver, cloudy swelling of the viscera, fragmentation of the heart muscle, bronchopneumonia, acute fibrinous pleuritis, chronic interstitial pancreatitis, slight arteriosclerosis. Atheroma of aorta.

Pancreas: In the gross appeared normal. Microscopically there was considerable fatty tissue between the lobules. Parenchyma were well-preserved. There was some increase of the interstitial tissue in places. The islands were not noticeably increased in number. Some of them were normal, but at least half of them showed more or less extensive hyaline degeneration. In some there had been almost complete destruction of the island cells. A few islands were hypertrophied. Arterioles were thickened.

Liver: Swollen and cloudy. Gall-bladder and ducts were normal. Microscopically there was considerable postmortem change. Vacuoles were numerous. There was well-marked focal necrosis, generally about the central veins.

Kidneys: Measured 11 x 5.5 x 3 cm. Fibrous capsule slightly adherent. Surface and cut surface appeared normal. Microscopically there was some granular degeneration of the tubular epithelium (probably postmortem); hyaline glomeruli were numerous. Arterioles were thickened.

CASE V.—H., male, aged thirty-seven years. Admitted to New York Hospital complaining of pain in abdomen and diarrhea.

Physical examination (on admission) showed the liver enlarged, edge $9\frac{1}{2}$ inches below costal margin, firm but not tender. Patient's head was considerably enlarged, and there was marked bulging of the left eye. Patient was in the hospital about a year. Repeated examinations of the urine showed a trace of albumin and hyaline and granular casts, but no glucose.

Clinical Diagnosis: New growth of liver.

Autopsy 4465. Anatomical diagnosis: Tumor (endothelioma?) of the left orbit; metastases in liver, kidneys, pancreas, lungs, heart, bronchial, and retroperitoneal lymph glands; abscess of the lung, acromegaly, arteriosclerosis.

Tumor of the Orbit: Right orbit contained a tumor the size of a bantam's egg, situated between the base of the orbit and the optic nerve, easily removed, adherent to sheath of optic nerve; consistence firm; cut surface was grayish pink and granular. Eyeball pushed forward; base of orbit was slightly eroded.

Microscopic Examination: The tumor was composed of alveoli filled with small, flattened endothelial cells, with large chromatic nuclei and small amount of pale cytoplasm. In some places the connective tissue was scanty and the alveoli large; in others the stroma was very abundant and richly vascularized and infiltrated with cords of tumor cells.

Liver: Greatly enlarged, and contained many small tumor nodules.

Microscopic Examination: Sections through tumor nodules differed in no way from those of original tumor.

Pancreas: There were numerous small tumor nodules in the pancreas similar to those in the liver. The tail of the pancreas, though free from tumor, appeared rather firm. Ducts were patent. Microscopically there was a slight increase of connective tissue in some places about the ducts, elsewhere the stroma as well as the glandular acini appeared normal. At least three-quarters of the islands of Langerhans showed hyaline degeneration, which in some cases was advanced. Islands were hypertrophied. Arterioles were slightly thickened. Larger ducts showed adenomatous hypertrophy of lining epithelium. Metastases composed of tumor cells, similar to those in liver. In places they completely surrounded the islands, which may have been normal or hyaline.

Kidneys: Weight (together), fifteen ounces. Upon stripping off the capsule small tumors were seen projecting above the surface, which was otherwise smooth. On section the markings were indistinct. Tumor nodules were scattered through the cortex; pyramids appeared normal. Microscopically there was granular degeneration of the tubular epithelium; a few of the glomeruli showed hyaline degeneration. Glomerular capillaries thickened. Tumor nodules were similar to those described above.

Hypophysis: Enlarged, size of small walnut, and soft.

Microscopic Examinations: Section showed a richly vascularized connective tissue supporting a large number of solid glandular tubules containing rounded or flattened epithelial cells. Occasional hollow tubules lined with low cuboidal cells and filled with colloid material were observed.

CASE VI.—H. T., female, aged forty-nine years; colored. Admitted to the Johns Hopkins Hospital for chronic nephritis.

Autopsy 2895. Anatomical diagnosis: Chronic diffuse nephritis (large white kidney), cardiac hypertrophy and dilatation, diffuse myocarditis and fatty degeneration; verrucous tricuspid, and aortic endocarditis, hemorrhagic gastritis, catarrhal enteritis, general anasarca, edema and atelectasis of lungs, myomas of uterus, pelvic peritonitis, general arteriosclerosis, chronic pancreatitis, colloid goitre, obesity.

Pancreas: Normal in size and consistence. Cut showed distortion of lobules. Ducts were dilated and a little thickened.

Microscopic Examination: There was considerable increase of the interstitial tissue, with atrophy of many of the acini. Islands were fairly numerous. Insular capillaries were thickened. A considerable number of the islands had undergone hyaline degeneration, and in some cases to an extreme degree.

Kidney: Microscopically there was extensive replacement of the cortex by fibrous tissue, with considerable granular degeneration and desquamation of the tubular epithelium. There were many hyaline and fibrous glomeruli. Well-marked thickening of the renal arterioles was observed.

Liver: Microscopically there was congestion of the lobules about the central veins, with some compression atrophy of the cells.

NOTE.—I am indebted to Dr. George H. Whipple, of the Johns Hopkins Hospital, and to Dr. William J. Elser, of the New York Hospital, for pathological material and for permission to report two of the cases included in this study.

ALCOHOLISM AND EPILEPSY, ALSO SO-CALLED ACUTE ALCOHOLIC EPILEPSY.¹

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THE craving for alcohol and alkaloids or substances that are similar to these in their action is so universal as to appear almost

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instinctive. From cereals, fruits, plants, seeds, and tubers, man has obtained substances for such use, and those commonly employed have been the various alcoholic beverages, cocoa, coffee, guarana, hemp, kola bean, maté, opium, tea, and tobacco. Such substances have been drunk, chewed, smoked, inhaled, used subcutaneously, and otherwise introduced locally. Habits of this kind were in vogue among the ancients even in the earliest times. There are records that tell of the use of wine 5000 B.C. And since it appears that man always has craved something to soften his sorrows and to add to his pleasures, there is no likelihood that we shall become absolutely free from this human weakness.

Having, then, these habits always with us, it is of the utmost importance to be familiar with the harm that results from such indulgence. This is a difficult problem, for upon no subject within the domain of medicine do such extreme views obtain as upon that of the use of intoxicants. Of all habit-engendering substances, alcohol is the one most commonly used, but a number of factors must be borne in mind in determining the effects produced by such use. The quantity and the quality of the liquor; the time of day taken, and the period of time over which it is consumed; and not the least important factor is the physical and mental make-up of the individual. The matter of tolerance is significant. It has been defined by Hare, of England, "as the capacity to ingest relatively large amounts of alcohol without experiencing the ordinary obtrusive physiological effects."

Although we know that at times alcohol may be used in enormous quantities and for a long period without showing appreciable deleterious effects, we also know that it may cause death acutely or it may bring about widespread degeneration through years of excessive indulgence. The pathological changes extend to all tissues except bone, but its effects are especially marked in the nervous system. The particular affinity of alcohol for this part of the body is shown even after death, when it may be found in the cerebrospinal fluid after all trace has disappeared elsewhere. In the nervous system both functional and organic disturbances are observed. Mental manifestations with alcoholism as a factor are especially numerous, and any type of insanity may be simulated. However, the only mental disorders which are distinctly the result of the prolonged action of alcohol upon a previously normal brain are delirium tremens and polyneuritic psychosis (Korsakow's disease), and even the latter is occasionally produced by the absorption of septic matter, and it is also said to have followed influenza and typhoid. All other psychoses occurring among alcoholics are of the types of those developing among abstainers.

Many believe that in the offspring of alcoholists there is a proneness to hysteria, insanity, idiocy, epilepsy, and crime. But here it is important to remember that the nervous instability which may

have led the parents to drink, may also account, at least in part, for these disorders and diseases developing in the offspring.

At times information is gathered that is worse than useless; it is misleading. Mott, a distinguished English writer, says: "The great point in any scientific observation is not to try to prove something, and to avoid any propagandistic tendency, thus the question of alcohol and insanity is an illustration in point. The Council of Fifty in Massachusetts investigated the number of patients admitted to asylums in which there was an alcoholic history; it was then suggested that they might investigate the number of total abstainers; it was found that they were quite as numerous."

Of special interest is the relation of alcoholism to epilepsy; it is concerned with this disease in several ways, and yet it probably is not as potently a factor in the causation of epilepsy as is often stated, for we have not sufficiently taken into consideration the nervous instability which frequently has led the parents to drink, and which in itself must have been partly, and at times perhaps wholly, responsible for the development of epilepsy in the offspring. It also appears that only rarely does chronic alcoholism produce recurrent attacks of fits, except as they are dependent upon the immediate taking of alcohol. This latter subject will be considered somewhat in detail later.

Alcoholism has, or is alleged to have, the following relations to epilepsy:

1. Drunkenness of one or both parents at the time of conception has been said to be a fruitful cause of epilepsy in the offspring (Esquirol). This is an exceedingly difficult matter to investigate, as the nature of the sexual act forbids observation. However, there is data which indirectly throws light upon this subject. In France it is said that a considerable number of children appear *nine months* after seasons of drinking, such as carnivals in the cities and church fairs in the country. It has also been observed in some countries that the congenital epileptics and imbeciles are conceived at the time of new wine. It is held, as a rule, in the wine countries that a poor school year comes seven years after a good wine year.

2. That injuries to the head in alcoholists may give rise to true epilepsy is stated by Oppenheim. This is quite possible just as alcoholism plus traumatism may cause insanity; and also, a blow upon the head in a syphilitic may act in the same way.

3. Chronic alcoholism in the parents may lead to epilepsy in the offspring; while reliable statistics are here wanting, it is probable that this is often one of the factors in the production of epilepsy.

4. Chronic alcoholism in the individual may lead rarely to epilepsy in those with no inherited or inherent tendency to the disease. This surely does not often follow except in cases of senile

epilepsy, where the attacks are rather an epileptoid manifestation and dependent upon an arteriosclerotic basis. Such attacks are less frequent and less severe, and the mental failure is not so marked, the condition also yields somewhat more satisfactorily to treatment than does the idiopathic disease.

5. In an epileptic who becomes an alcoholic, the attacks are increased in number and in severity. Of the marked intolerance of epileptics to alcohol, there can be no question. All epileptologists have met with instances where the disease has undergone a remission and where attacks have been again precipitated by the taking of alcoholic beverages.

6. Alcoholic drinks may be sought by epileptics because of post-epileptic depression, and there may be little or no drinking at other times. The disease, of course, is exaggerated.

7. A few epileptics upon becoming aware of the dreadful malady with which they are afflicted, have plunged into drink and greatly aggravated their disease; and this, independent of the depression which is sometimes the direct result of the attacks. Here, epilepsy is the exciting cause of alcoholism.

By those in charge of alcoholic wards in hospitals, the phenomenon of convulsions is frequently observed. This may be due to uremia, and it also occurs in epileptics who have gotten drunk. But there is another variety of convulsive disorder seen, and this has received but little attention at the hands of writers upon alcoholism; some even fail to mention it. We refer to so-called acute alcoholic epilepsy. The term "epilepsy" is here unfortunately used, since these attacks have no more relation to epilepsy than have the convulsions so commonly seen in children. As a rule, there is but little albumin in the urine of these patients, and this usually clears up in a few days. Contrary to the belief of a number of physicians, alcoholic convulsions and delirium tremens appear in most instances to be abstinence phenomena. They do not usually occur together, although occasionally this is observed. It is argued that these two diseases sometimes develop while the patient is still drinking heavily; in some of such cases perhaps there has suddenly developed a catarrhal condition which has prevented the absorption of alcohol; or it may also arise through a patient being profoundly intoxicated and therefore not conscious enough to continue drinking. These fits are most apt to occur in continuous alcoholists in whom a rather high degree of tolerance has been attained, and they are most likely to obtrude themselves during the first twenty-four hours of abstinence. When attacks of delirium tremens are present they occur a little later. These convulsions are not preceded by insomnia, tremor, and fear unless they are accompanied by delirium tremens. The attacks bear considerable resemblance to genuine epileptic seizures. They are mostly major; an injury may be sustained by falling, unconsciousness is complete, the tongue at times is bitten, sleep often follows

the attack, and the patient usually awakens with a headache. But still there is not the characteristic appearance of an epileptic, and the patient usually bears the stamp of a chronic alcoholic; the attacks seldom occur independently of drinking.

The prominence given alcohol as a cause of epilepsy has been overestimated, and this is apparent from the following: The nervous instability which at times drives parents to drink is in part responsible for the development of epilepsy in the offspring. We know that drinking is very common and epilepsy is relatively rare. Alcoholism is much more frequently encountered in males, but epilepsy at least is as common among females. Many of the cases of epilepsy have developed before the age when drink could be obtained. Insanity and nervous diseases are common among the Jews; epilepsy is frequently seen, and yet the Jews are an abstemious people. Those of us who have done special work among alcoholics know that a drunken Jew is a great rarity. The report of the Craig Colony for Epileptics for 1912 gives alcoholism as the probable cause of epilepsy in less than 1 per cent. of the admissions for that year, 227 patients were admitted. And, finally, even those alcoholists with no inherited or inherent tendency to epilepsy, who have convulsions (so-called alcoholic epilepsy), almost never have fits independent of drinking.

A great deal is heard about the rapid increase in the number of epileptics, but the writer believes here we stumble against some of the errors which have arisen in estimating the number of insane. It is only in recent years that we have had special institutions for the care of epileptics so that we are only just beginning to obtain data from which to draw more definite conclusions as to etiology. The conditions conducive to epilepsy and insanity may not parallel each other, but they probably do run in much the same direction.

The writer knows of no reason for believing that through racial degeneration, insanity is increasing rapidly, and this, perhaps, is worthy of a moment's consideration. Years ago it was thought to be more of a disgrace to go to an asylum or sanitarium than it is today; the insane are now infinitely more humanely cared for than formerly, and there is less fear among the relatives about having one of their family leave home; therefore, many are now available for statistics which were formerly missed. The horrors that existed in the so-called mad-house are familiar to us all, patients were chained to the walls, they were otherwise abused, and death frequently resulted from accidents, houses of detention were unsanitary, and many died because of such unhygienic conditions.

I think it probable that there is a slight relative increase in the number of insane, and this, in a measure, may be accounted for through our present scientific care of weaklings; thus, children are kept alive today who years ago could not have lived, and consequently we have the survival of the unfit, some of whom are imbecilic, epileptic, degenerate, and insane.

REVIEWS

DENTAL ELECTROTHERAPEUTICS. By ERNEST STURRIDGE, L.D.S. England, D.D.S., Fellow Royal Society of Medicine; Member British Dental Association, London, England. Pp. 318; 154 engravings. Philadelphia and New York: Lea & Febiger, 1914.

THIS last of the series of small text-books on various phases of dental practice published by Lea & Febiger is a comprehensive treatise on electrotherapeutics. Inasmuch as the author believes that no one should employ this therapeutic agent without fundamental knowledge of electricity and electrophysics, the first half of the work gives a brief but satisfying discussion of the underlying principle of electric energy and the means of employing it. In this section is also included a description of the ordinary electric apparatus of the dental office, embracing all but the most recent additions to the dental outfit.

The chapter on x -rays describes the extensive field for the radiographic work in dental practice together with the technique for making radiographs. The author justly emphasizes the rapidly enlarging field of usefulness of x -rays in the diagnosis of the condition about the root apices of pulpless teeth and in ascertaining the direction of the root canals and the correct or insufficient filling of the same. His experience accords with that of the majority of practitioners who have employed it, for he considers the therapeutic value of x -rays limited in dentistry.

The most valuable therapeutic use of electricity recommended by the author is in ionic medication, in which field he is one of the pioneers. Testimony is gradually increasing as to the effective use of ionization in the germicidal treatment of many dental infections, and particularly in those low-grade peri-apical infections which yield so unsatisfactorily to other treatment. This with ionic medication of pockets about the teeth affected with pyorrhea alveolaris offers an additional valuable agent in the fight for the extermination of localized infections in the mouth, which are so generally recognized as the original foci of infections occurring in other portions of the body. Besides the germicidal action locally, the author suggests that the improved conditions may have resulted because "the dead organisms were absorbed into the blood stream

and had an effect upon the opsonins similar to that of vaccine prepared from cultures." For practitioners, the book may be recommended as a useful hand-book upon the subject of dental electricity, and should prove useful as a college text-book.

C. R. T.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Vol. III, No. 1, February, 1914. Pp. 190; 91 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THIS number opens the third volume of this popular periodical. It is prefaced by a note explaining that many of the cases referred to in the present number have already been reported in past numbers of the *Clinics*, and that the same can be said in regard to the skiagrams and photographs illustrating these cases; but their reappearance is accounted for by the fact that the patients or the figures illustrating their cases were shown by Dr. Murphy at the Clinics he held during the Clinical Congress of Surgeons last November. There is appended an advertisement of the days and hours of Dr. Murphy's Clinics at Mercy Hospital.

It might have been expected that Dr. Murphy would seize upon the present as an opportunity to assemble his clinical material and to report his operative results with more accuracy than has yet appeared; the reader is disappointed, however, to find that as he increaseth knowledge he increaseth sorrow, and that there is no new feature in Murphy's *Clinics*. The isolated cases reported almost uniformly show brilliant results; but in spite of the wealth of material there is no evidence of an attempt to allow the reader to draw a conclusion to the whole matter, by marshalling before him in orderly array facts on which his judgment may be based. Instead of this, there is endless repetition of catchy phrases and colloquial aphorisms, with Dr. Murphy's conclusions; but what the thoughtful reader desires now is to justify these conclusions in his own mind, and not to accept them on the unqualified ground of *ipse dixit*—especially when they are at war with popular beliefs.

There are several interesting addresses included in the present number of the *Clinics*, the most charming of which is that given by Sir Rickman Godlee (the editor calls him simply "Sir Godlee"), with the title "Lord Lister and Antiseptic Surgery." Of much interest also is Mr. Herbert Paterson's address on "Gastric Ulcer and Gastric Carcinoma."

A. P. C. A.

CASE HISTORIES IN PEDIATRICS. By JOHN LOVETT MORSE, A.M., M.D., Associate Professor of Pediatrics, Harvard Medical School; Associate Visiting Physician at the Infants' Hospital and the Children's Hospital, Boston. Second edition, 639; 200 case histories; freely illustrated. Boston: W. M. Leonard, 1913.

THIS book forms one of the "Case History Series" by Boston authors, which follow the very desirable precedent set by Dr. Cabot. They are intended as supplemental adjuncts to systematic textbooks. The subject of pediatrics in its most important aspects is well covered from the author's personal experience. The book begins with an introductory section upon the normal development and physical examinations of infants and children—a model of conciseness, yet fully comprehensive. The case histories, which form the bulk of the work, are divided into the more or less usual classifications: diseases of the newborn, diseases of the gastrointestinal tract, etc. In each case the salient points of the history are first presented, followed by the results of careful physical examination. Up to this point no intimation is given as to the diagnosis except from the general heading, and the reader will find excellent opportunities for practice in inductive clinical reasoning. Then follows the author's diagnosis and the reasons therefor, with the prognosis and the treatment employed. By omitting all attempts at classification in the text and inserting the case histories in heterogeneous order, this slight aid to diagnosis would be denied and the reader's diagnostic acumen would be severely tested. The disadvantage of sacrificing all system could be obviated in the index, where the cases could be indicated by their special numbers and pages under proper classification for the use of those who desired to study this or that class of disease. In the preface, the author states that the diagnoses are correct in every instance in which they are stated with positiveness. As these comprise the great majority of cases, the objection to their unqualified acceptance is obviated. As a matter of record, a short note as to positive results—recovery, death, or whatever they may have been—would appear more convincing, since prefaces, unfortunately, are not always read. Throughout the book the didactic method of presentation is employed even to the point which at times might be considered unwarranted. The author's reasoning, however, is always logical, and were it not for the fact that human ills are not invariably subject to such treatment, no possible criticism could be made. On the other hand, he avoids *in toto* the most unsatisfactory and perhaps more dangerous habit of diagnostic vacillation. To the student, and even more to the practitioner of medicine, no more valuable accessory training in the subject of pediatrics could be recommended.

J. C. G.

HISTORY OF MEDICINE. By FIELDING H. GARRISON, A.B., M.D., Principal Assistant Librarian, Surgeon-General's Library, Washington, D. C. 763 pp.; about 200 portraits. Philadelphia and London: W. B. Saunders Company, 1913.

THIS book is one of the most interesting and valuable of recent additions to medical literature, and meets adequately the demand that has long existed for a fuller one-volume history of medicine in English.

The author has given a scholarly and delightfully entertaining account of the development of medicine from the earliest times to the present year, with brief mention or longer sketches of about twenty-five hundred of the greater men of medicine. To the more important of these, he gives three or four pages of biography, and portraits of about two hundred. A feature of the book is the amount of space assigned to recent medical history, almost half the book being occupied with the nineteenth and twentieth centuries. Sketches of many of the men in this country and Europe at present most active in the advancement of medicine are here to be found. References to the literature are appended in footnotes throughout the work to the number of two or three thousand.

In an appendix are included a chronological table of 1700 important events in medicine, a critical review of other works on the history of medicine, the references to biographical sketches of one hundred of the most important men in medicine, and bibliographies of about sixty-five subjects related to the history of medicine. There is a complete index of all the personal names and all subjects mentioned in the text.

As a work of reference, this book is, of course, quite invaluable, and constitutes a mine of information; but it is more than this, for the author has presented his material so entertainingly that most delightful hours may be spent in reading the book from cover to cover.

J. H. A.

PATHFINDERS IN MEDICINE. By VICTOR ROBINSON. Pp. 317; 16 illustrations. New York: Medical Reviews of Reviews.

It is well for the medical profession that Victor Robinson overcame a hitherto generally "regarded psychological prejudice" against taking advice and yielded to the suggestion of his medical colleagues, to publish this present volume of biographical sketches. The latter, in part, have appeared in various medical periodicals, but as isolated essays they were doomed to extinction, if not oblivion, having been almost swallowed up in the torrential flood issuing continuously from the press. Published now for the first time in a

the head of stomatology, in an eminently concise and practical manner. The book is intended not so much for the specialist as for the general medical practitioner, and should be of almost daily service to the latter in his constant meeting with what he has hitherto regarded as obscure mouth conditions. Rational treatment of nearly all the oral lesions described is well within the power of the general practitioner. The original matter in the book includes the dietetic preventive treatment of dental caries, methods of treating pyorrhea alveolaris, a simple appliance for fixation of fragments in fracture of the jaws, and a method of recording examination of the teeth of school children.

Chapters VII and VIII, on the preventive treatment of dental caries, are the most important in the book, and form an epitome of what is perhaps the most valuable original work ever done on the subject.

In an otherwise excellent chapter on fractures we regret that the author does not mention fixation of the lower teeth to the upper with a metal intermaxillary splint for fractures posterior to the last molar. This method is unequalled for maintaining correct occlusion.

The author evidently has had little experience with ether anesthesia as practised in this country, as shown by his objection that "special apparatus" is required.

In an appendix are given numerous formulæ useful in the treatment of oral diseases, and also a list of simple dental instruments that should be in the cabinet of every general practitioner and hospital dispensary.

The book is almost a pioneer in a subject that we hope will gain before long the regular notice that it deserves from medical teachers and practitioners.

R. H. I.

THE PRESCRIBING OF SPECTACLES. By ARCHIBALD STANLEY PERCIVAL, M.A., M.B., B.C. (Cantab.), Senior Surgeon, Northumberland and Durham Eye Infirmary. Second edition. Pp. 168. Bristol: John Wright & Sons, Ltd. London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd.

THE second paragraph of the optical section contains the statement, "I shall assume in this section that the reader is familiar with the elements of the subject." This sentence might appropriately have been placed at the beginning of the book, for the subject as here presented can only be grasped satisfactorily by a reader already acquainted with the principles of refraction. Most of the matter is, of course, common knowledge. The justification

for a restatement consists almost entirely in the manner of the presentation of which the first essential is clearness. In this respect there is little to be criticized, if the reader comes properly prepared, but it is not a book for the novice.

We note that the author prefers the concave to the plane mirror in retinoscopy; he recommends that 1 D be deducted from the total H found under atropin and about 0.75 D when homatropin is used. Allowance for range is not mentioned. Full correction of myopia is very properly recommended, as is also the fogging system in the subjective examination. The two-thirds rule is explained for the correction of presbyopia, which latter term the writer would do away with, holding that if it is used at all it should include acquired hypermetropia as well as defective accommodation.

T. B. S.

KLINISCHE BAKTERIOLOGIE UND PROTOZOENKUNDE. By DR. JULIUS CITRON, Assistenten der II Med. Klinik der Univ., Berlin. Pp. 172; 65 illustrations, 7 colored plates. Leipzig: Klinkhardt.

THIS small German manual gives in brief form a description of the common laboratory procedures in bacteriology and protozoölogy with a short description of the common organisms encountered. The illustrations, especially the colored plates, are rather diagrammatic. Bacteriologic technique (including staining methods, preparation of media, animal inoculation, securing of fluids for examination) is discussed, but only in barest outline so that the worker would search in vain for many minor details of considerable practical importance. Similarly in the discussion of the various organisms only the most important are considered and the description of these is brief. For those wishing a German manual this work would compare favorably with any of the smaller less pretentious works on the subject, but it has no advantage over many English manuals.

J. H. A.

A COURSE IN NORMAL HISTOLOGY. By RUDOLF KRAUSE, Professor of Anatomy at the University of Berlin. Translated from the German by Philipp J. R. Schmahl, M.D. 2 volumes; 86 pages, 406 pages; 30 illustrations and 98 colored plates, after drawings by the author. New York: Rebman Company, 1913.

THE German original of this book appeared in 1911, and was notable for its excellent illustrations in colors, and the author's

extensive use of the frozen section method as a routine class procedure in normal histology. In the translation, the work appears in two volumes; a smaller, devoted to microscopic technique, and a larger, in which the subject proper is taken up. The colored plates are the product of the original press, and are of the same excellence as in the German edition.

The volume on microscopy contains directions for all procedures necessary to study tissues. The descriptions are for the most part precise and lucid, and many hints of a practical nature show the first-hand experience of the author. The method followed in the second volume is to give descriptions of each plate independently, as in an atlas. These descriptions include not only the histological details seen in the illustrations, but also the method of preservation of each tissue, and its after-treatment. Of the 208 illustrations, 178 are from mammalian tissues, and about half of these are from human material. These include a comprehensive series of tissues, although the author has apparently thought it unnecessary to show the corpus luteum of the ovary, the Purkinje fibres and atrio-ventricular bundle of the heart, and the parathyroids, all of which are of great interest at the present time. Most of the sections were obtained by the freezing method, and stained by the Biondi solution, for the preparation of which very special directions are given. These and other departures from stereotyped methods give the work a considerable degree of originality, and make it an attractive exposition of the subject. W. H. F. A.

LEITFADEN DER PRAKTISCHEN MEDIZIN, Bd. 7, INNERE MEDIZIN.
By GEORGE ZUELZER, M.D. Pp. 367. Leipzig: Dr. Werner Klinkhardt, 1913.

THE second and larger volume of Zuelzer's *Innere Medizin* completes the medical portion of Bockenheimer's series of hand-books, designed at a low price to cover the present status of the whole subject of Medicine.

The volume under review covers in 346 pages the diseases of the digestive and urinary tracts, of the spleen, thyroid and blood, and diseases of metabolism. It is obvious, therefore, that the subjects can only be treated superficially and yet it is surprising to see how many facts can be condensed into such small space. Numerous laboratory tests are given in satisfactory detail; but symptomatology and diagnosis is often disposed of, perhaps necessarily, in a few, dogmatic sentences. Diseases of the spleen, for instance, are dismissed in one page, no mention being made of Banti's Disease or any type of primary splenomegaly. A complete and correct

index is a valuable feature. Frequently condensation has been carried to such an extent that treatment has been entirely omitted. It is difficult, therefore, to see the value of such a hand-book, which, from its many omissions, becomes unsatisfactory for reference, and untrustworthy for study. As the "latest out" and at a low price, it might, however, have some vogue in Germany, but in this country this demand can be supplied in other and better ways.

E. B. K.

UBER LAPARO UND THOROKOSKOPIE. By H. C. JACOBÆUS, M.D., Privat-dozent in Stockholm. Pp. 170; 5 tables and 1 illustration. Würzburg: Curt Kobitzsch, 1913.

ALTHOUGH Kelling as early as 1902 directed attention to the feasibility of examination of the closed body cavities, especially the peritoneal, by the use of electrically lighted instruments, the author of this monograph must be classed as the true pioneer from the standpoint of modern practicability. He has divided his energy between examinations of the abdominal and thoracic cavities, and after detailing the technique, which is very simple to one at all familiar with endoscopy, states the indications for the procedure, claiming that not infrequently the method could and should be adopted for the exact diagnosis of obscure or uncertain pathological lesions of the abdomen and thorax. The author narrates in detail the histories and findings in 140 cases examined in this manner, and has succeeded in establishing the differential diagnoses in the following conditions: cirrhosis of the liver, Pick's disease, syphilitic liver, congestion of the liver, tuberculous peritonitis, abdominal tumors, acute and chronic exudative pleuritis, thoracic empyema, and artificial pneumothorax. The work is supplemented by tables showing very excellent photographic and colored drawings of the pathological structures studied.

B. A. T.

DISEASES OF WOMEN. By THOMAS GEORGE STEVENS, M.D., B.S., F.R.C.S., M.R.C.P., Obstetric Surgeon, with charge of out-patients, St. Mary's Hospital, Paddington. Pp. 431; 202 illustrations. London: University of London Press.

IN this book Dr. Stevens has given us his ideas based upon ten years' experience as a clinician and a teacher of gynecology. The subject matter has been classified according to a compromise between clinical manifestations and purely pathological processes.

The later theories of the physiology of menstruation and the disorders of this function are given fully. Here as throughout the book all controversial points are impartially discussed.

A section is devoted to the anomalies of pregnancy, the pathological results of which are commonly met with in gynecological practice. An interesting and helpful chapter is included on the general conditions associated with pelvic disorders and the relation of these conditions to gynecological diagnosis.

Newgrowths of the generative system are considered at length. The author mentions but does not recommend x-ray or radium therapy in the treatment of fibroid tumors of the uterus. The advantages and the technique of the Wertheim Operation for carcinoma of the cervix are concisely presented. The necessity of a thorough pelvic examination for the early diagnosis of possible malignant disease in cases of irregular uterine hemorrhage is emphasized.

The author concludes with short but complete chapters on the preparation of patients, the after-treatment, and postoperative complications of gynecological conditions.

The book contains a minimum of typographical errors, and it should meet with no small measure of popularity. P. F. W.

DIE GOLDSCHMIDTSCHES IRRIGATIONS-URETHROSKOPIE. By Dr. A. SCHLENZKA. Pp. 99; 24 illustrations and 12 tables (6 in color). Leipzig: Dr. Werner Klinkhardt.

IN this masterfully composed little book the author has paid an appropriate literary tribute to the memory of his teacher, Dr. H. Goldschmidt, of Berlin, the father of "irrigation urethroscopy." It is doubtful if Goldschmidt himself could have presented a more complete, systematized, and summary exposition of his crowning life-work.

The author briefly reviews the development of urethroscopy, delineating the improvements in construction of anterior, posterior, and combined urethrosopes, including the urethrocystoscope. The technique of examination is carefully considered and the appearance of the normal and pathological urethra accurately described. The cuts illustrate well the parts and mechanism of the Goldschmidt instruments, and the plates, six of which are in color, at the end of the monograph, amply and satisfactorily, represent the various views of the urethra in health and disease.

The final chapters are devoted to a consideration of operative treatment, including instillation, electrolysis, ignipuncture, cauterization, and prostatic incisions, for the performance of which the Goldschmidt urethroscope is well equipped and adapted.

B. A. T.

A DICTIONARY OF MEDICAL DIAGNOSIS. By HENRY LAWRENCE MCKISACK, M.D., M.R.C.P., London; Physician to the Royal Victoria Hospital, Belfast. Second edition. Pp. 590; 76 illustrations. New York: William Wood & Co.

THE first edition of this book appeared in 1907. Since then there have been numerous advances made in the science of diagnosis. The description of many of the newer signs, reactions, and tests has been incorporated in the present edition. The general character and scope of the book is unchanged. The various symptoms and physical signs occurring in disease are arranged in alphabetical order. The list also includes descriptions of the more usual laboratory methods of diagnosis, of *x*-ray diagnosis, and of a few of the many instrumental methods that may be employed in determining the cause of disease. In the last category no mention is made of the findings achieved by the use of such valuable instruments of diagnosis as the electro-cardiograph in heart disease, the cystoscope in diseases of the genito-urinary tract, and the proctoscope in diseases of the lower portion of the alimentary canal. The gastroscope is dismissed as worthless and the bronchoscope not mentioned at all.

For the most part the description of the various symptoms and signs are concise but clear and complete. Criticism might be made of the author's classification of the various arrhythmias and particularly might fault be found with the omission of any mention of auricular fibrillation. The sections on examination of the blood, sputum, and urine are most commendable. In general the book will be found useful for quick superficial review and for reference.

J. H. M., JR.

TEXT-BOOK FOR NURSES: ANATOMY, PHYSIOLOGY, SURGERY, AND MEDICINE. By E. W. HEY GROVES, M.S., F.R.C.S., Assistant Surgeon, Bristol General Hospital, and J. M. FORTESCUE-BRICKDALE, M.A., M.D., Assistant Physician, Bristol Royal Infirmary. Pp. 407; 205 illustrations. London: Oxford University Press.

IN presenting this text-book for the use of nurses the authors have taken a long step forward in making possible the standardization of nursing knowledge and efficiency. It is in no sense a hand-book on nursing. No attempt is made to tell *how* details are to be executed, the whole emphasis is laid on *why* such measures are necessary. The aim is to arouse the intelligence of the nurse and make her work a conscious scientific effort.

The foundation which makes this possible is the section on anatomy and physiology. The section on surgery is wisely opened

with a concise review of the principles of bacteriology and the relation of microorganisms to disease. The main field of general surgery is covered, and symptoms reduced to a physiological and anatomical basis. The section on medicine covers the subject in a brief and satisfactory way. The care taken in the preparation of this book is evident throughout.

A. A. H.

THE EVIL EYE, THANATOLOGY AND OTHER ESSAYS. By ROSWELL PARK, M.D., LL.D. (Yale). Pp. 380. Boston: Richard G. Badger, The Gorham Press.

ALL lovers of history and students of essays will heartily welcome the publication of this series of essays by Rosewell Park. Thirteen in all, they cover subjects of wide range, dealing with mythology; studies of signs and symbols; the foundation of Christianity and its relation to the Grecian mysteries; the relation of the Church to medicine; a critical but speculative inquiry into the mystery of death; biographical sketches of famous men; and several essays covering in interesting fashion certain historical aspects of medicine.

Possessed of a facile pen, an ease of expression, coupled with his wealth of knowledge the author has undoubtedly created an enviable niche for himself in the field of literary endeavor.

B. B. V. L.

ESSAYS ON GENITO-URINARY SUBJECTS. By J. BAYARD CLARK, M.D., Assistant Genito-urinary Surgeon to Bellevue Hospital. Pp. 174. New York: William Wood & Company.

THE author has presented ten short chapters on variously chosen subjects of genito-urinary interest. About one-half of the contents is composed of previously read and published papers, some as far back as seven years, each chapter so constituted bearing supplementary notes in an attempt to bring it up to date. As a whole, the subject matter is not without interest, but the object of the presentation is not clear, since to students or those unfamiliar with genito-urinary knowledge, the cursory manner of the essayist will convey little of fundamental value, while to the skilled clinician, the incompleteness of the subjects treated stands out prominently, adding not only nothing new, but omitting certain considerations of importance.

In discussing the diagnostic advantages of the cystoscope, the essayist slights a number of vesical conditions, among them tuberculosis, claiming that they are not to be included in "affections ordinarily requiring surgical intervention."

The author elects to base functional kidney diagnosis on ureteral catheterization, an act occasionally impossible of accomplishment. He ignores absolutely the kidney test by indigocarmin, whereby the functional sufficiency of the kidney may be gauged when it will be impossible by any test dependent upon bilateral ureteral catheterization. Moreover, the phloridzin test, which is recommended, has been proved to be unreliable, no glycosuria occurring even from normal kidneys.

Exception may also be taken, rightfully, as to the advisability of catheterizing the supposedly normal ureter through a bladder infected by descending tuberculosis of the other side. Likewise the urine separator or segregator has today few advocates. Other doctrines are seriously questionable, as for example, in addition to massage, the treatment of chronic prostatitis by such measures as electricity and the mechanical application of heat and cold.

B. A. T.

THE SEXUAL LIFE OF THE CHILD. By ALBERT MOLL, M.D.
Translated from the German by EDEN PAUL, M.D. Pp. 339.
New York: The Macmillan Company.

THE translation of this work, coming as it does, at a time when such general interest is being taken in eugenics, promises to fill a want felt until now in the preparation for this field of activity.

The author points out that the rational solution of the problems of eugenics must be based on fact and that this definite knowledge, in so far as the normal sexual life of the child, at least, is concerned, has as yet been neglected. The subject is then put before the reader in a systematic and comprehensive way. Every physician, teacher, parent, and social worker should have the information contained in this book at his disposal.

A. A. H.

SEX—ITS ORIGIN AND DETERMINATION. By THOMAS E. REED, M.D. Pp. 313. New York: Rebman Company, 1913.

HAD this book appeared a decade ago, it would have received more attention than at the present day. The observations contained therein were first stimulated by the remarks of Darwin, that, as all present-day animals are descended originally from tide-water organisms, there might exist cycles in some of our life processes, which could be looked upon as the persisting effect of these tidal movements. The author believes that he can trace this effect in, among other phenomena, the "functional phases" of parturition and the alternating male and female phases of the ova, which, as

he believes lead to the determination of sex. To refer more specifically to the latter, he says that if the ovum is fertilized during the ebb of the tide, the offspring will be of one sex, and if during the flow of the tide, of the other sex. Moreover, he assures us that his observations bear out his contention.

On the other hand, the evidence is rapidly accumulating that the chromosomal dimorphism of the spermatozoa is the factor upon which sex determination depends, and a recent paper by Wodsedalek in the *Biological Bulletin* gives good evidence that somatic cells of the male and female have likewise different chromosomal constitutions. In view of these developments many of the ideas contained in this volume must be considered as of merely historical interest.

W. H. F. A.

BACTERIA. By DR. MAX SCHOTTELIUS, second edition translated by Staff Surgeon HERBERT GEOGHEGAN, R. N. Pp. 324; 10 colored plates and 33 illustrations. London: Oxford University Press and Hodder and Stoughton.

THE present volume represents the translation of the second edition of a previous popular work on bacteria. In this edition the text has been thoroughly revised and the inaccuracies of the first edition corrected. The chapters on "Immunity and Protective Vaccination" and "Protozoa" have been rewritten and enlarged to meet the modern views on these subjects. The work suffers the fault of many translations in being a little verbose and drawn out, but force and clearness are not sacrificed. The discussions are in more or less popular terms, so as to be clearly intelligible to the lay reader. The book, however, is intended for the physician or student of bacteriology, and will give to either a very good general idea of bacteria, their universal distribution in and their relation to various natural processes; it further treats of the manner of action of bacteria in disease with the possibilities and methods of combating diseases caused by them.

F. H. K.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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On the Quantity of Glucose in the Blood in Health and Disease.—B. PURJESZ (*Wien. klin. Woch.*, 1913, xxvi, 1420) has made a number of quantitative determinations of glucose in the blood in health and in various diseases. He finds that it varies between 0.0451 and 0.087 gm. per cent. in health, the blood being taken from the cubital vein in the morning, before food has been taken into the stomach. The normal variation is considerable, but, given like conditions in one and the same individual, there is little change in the quantity of sugar. Normally, the greater part of the blood sugar is in the plasma; only a trace is found in the erythrocytes. During febrile periods, the sugar in the red corpuscles may be increased. With increased activity of the thyroid gland, the quantity of glucose in the blood is small. Subcutaneous administration of the infundibular portion of the pituitary body in normal individuals increases the blood sugar. In Addison's disease, the sugar in the blood was found to be low. In the cases with hypertension examined, there was found a hyperglycemia. In pneumonia, fever was accompanied by hyperglycemia, though the latter was lacking in miliary tuberculosis and typhoid fever. Purjesz believes there is a fairly constant association of hyperglycemia with hypertension and fever.

Diabetes Insipidus and the Pituitary Gland.—M. SIMMONDS (*Munch. Med. Woch.*, 1913, lx, 127) reports an instructive case of diabetes insipidus. The patient, a woman of thirty-seven years of age, was operated on for cancer of the breast. She made a good recovery from the operation. The urine at this time averaged about 1500 c.c. daily, with specific gravity 1.012 to 1.015. Ten weeks after the operation,

the patient returned to the clinic and reported that for two weeks she had had marked polyuria and increase thirst. The urine varied in amount between 10 and 19 liters, the specific gravity between 1.002 and 1.003; there was neither sugar nor albumin. The patient suffered from extensive metastases and finally died three months after the operation. Autopsy revealed metastases in the skin, breast, liver, cervical, pectoral, and abdominal lymphatic glands, pleura, and vertebræ. The kidneys were normal. The cerebrum, cerebellum, and medulla were also normal; there was no enlargement of the ventricles of the brain. The posterior aspect of the sella turcica felt soft, and so the entire sella and pituitary gland were removed *en masse*. After decalcification, sections were prepared. Microscopic examination showed a metastasis involving the bone and the adjacent posterior lobe of the pituitary body. As Schäfer has shown that the anterior lobe has no diuretic properties, Simmonds explains the polyuria through stimulation of the pars intermedia by the presence of the malignant growth in the posterior lobe, which had been completely destroyed.

Eosinophilia in Carcinomatosis and in Lymphogranuloma.—R. STRISOWER (*Wien. klin. Woch.*, 1913, xxvi, 16) reports an eosinophilia which at one time amounted to 45.3 per cent. with total white count of 15,000 in a patient suffering with carcinomatosis, the result of primary uterine cancer. The red-blood corpuscles were 4,700,000, the hemoglobin 60 per cent. No nucleated red cells were found in the blood. Neither clinical study nor autopsy revealed any of the usual causes of eosinophilia. There were metastases in the sternum, and the marrow here was loaded with eosinophile cells. In a case of lymphogranulomatosis (Paltauf-Sternberg), an eosinophilia of 42.6 per cent. with total white count of 28,900 was observed. In this case there was a marked anemia, the red cells numbering 1,890,000, hemoglobin 35 per cent. A few erythroblasts were found. Autopsy showed great enlargement of the glands of the left side of the neck, also of the mediastinal, retroperitoneal, mesenteric and inguinal regions, with metastases the size of a bean to that of a cherry in spleen, liver, right adrenal, and bone-marrow. An excess of eosinophiles was found only in the bone-marrow.

On the Absorption Spectrum of Phenolphthalein.—B. BARDACH (*Wien. klin. Woch.*, 1913, xxvi, 141) has found that phenolphthalein in the urine, in amounts such as may occur after the administration of the drug as a laxative, may give rise to a single rather broad band in the spectrum situated about midway between D and E. As little as 0.004 gm. per liter of urine may give rise to the spectrum. In examining for the band, 0.5 c.c. of 15 per cent. sodium hydrate is added to 10 c.c. of urine. This is placed in a test tube 3 cm. in diameter and examined. The specimen should be examined while fresh, as the dye may disappear after a short exposure to the air. It is apparent that very small amounts of phenolphthalein may be detected in the urine—so small, in fact, that the color of the drug cannot be detected in the presence of the urinary pigments. The spectrum of phenolphthalein should be borne in mind in examining the urine for blood or urobilin. Reduced hemoglobin has a very similar spectrum. To differentiate

between urobilin and phenolphthalein, add a few drops of hydrochloric acid to the specimen and reëxamine. The spectrum of phenolphthalein is not seen in acid urine.

On the Partition of Cholesterin, Cholesterin Esters, and Lecithin in the Blood.—M. BUEGER and BEUMER (*Berlin. klin. Woch.*, 1913, l, 112) have made quantitative determinations of the free cholesterin, cholesterin ester, and lecithin in the blood serum in a number of diseases. They have apparently established the fact that free cholesterin is always present, though the proportion of total cholesterin which is free is variable. As a rule, free cholesterin amounts to at least 30 per cent. of the total. The highest value, 2.469 gm. per liter of serum, was found in severe cholemia, though high values were also encountered in diabetes with lipemia. Buerger and Beumer were unable to confirm the view expressed by Rohmann to the effect that sera rich in free cholesterin give a positive Wassermann reaction. In some cases with excessive amounts of free cholesterin, the Wassermann reaction was negative. As a rule, the quantity of lecithin parallels that of cholesterin. Here, too, it was found that a high lecithin content does not necessarily mean a positive Wassermann reaction.

The Dietetic Therapy of Urticaria.—H. SALMON (*Wien. klin. Woch.*, 1913, xxvi, 1399) has had excellent results with the dietetic therapy of chronic urticaria. He has never been able to convince himself of the value of calcium salts in the treatment of this condition; with the injection of normal human serum he has had no experience. The diet which Salmon has devised is poor in protein, as it is presumed that the urticaria is an anaphylactic phenomenon. Its frequent occurrence after eating lobster, cheese, eggs, strawberries, etc., is well known. The diet consists of tea or coffee with plenty of sugar, bouillon, lemon or grape juice, brown bread (*schrotbrot*) about 200 gm. with a liberal allowance of butter, rice, "Griess," barley, oatmeal, etc. (no legumens), cooked in bouillon or water with butter in abundance, green vegetables prepared like the cereals, potatoes, fresh or cooked fruits. This diet, the caloric value of which is enhanced by butter and sugar, is estimated to contain about 35 to 40 gm. of protein, a considerable portion of which is not absorbed. The urticarial eruption subsides strikingly, as a rule, after the second or third day of the protein-poor diet. Generally, it subsides entirely within the fourteen days during which the diet is continued. Usually, eggs, cheese, milk, and meats may now be added to the diet gradually without a recurrence of the urticaria.

On the Significance of Abderhalden's Serum Reaction in Psychiatry.—W. MAYER (*Münch. med. Woch.*, 1913, lx, 2044) reports his observations on Abderhalden's ferment reactions in a small series of psychiatric cases. He feels that paradoxical results are due to faulty technique. The serum of patients suffering with dementia præcox always contains a specific enzyme for the sexual gland (ovary or testis, according to the sex of the patient) and usually enzymes acting upon the cerebral cortex and the thyroid gland. In the group of functional psychoses, no specific ferments could be found in the blood serum—

a point which may prove to be of value in the differential diagnosis of dementia præcox and manic depressive insanity. Sera from general paretics contain a group of specific enzymes as a rule; there is always an enzyme which acts specifically upon the brain and usually enzymes for the sexual glands and liver, often for the thyroid as well. Thus, the only difference found between the sera of the paralytic and the patient with dementia præcox has been the presence of the liver enzyme in the former. Mayer believes the method is one which may prove valuable in psychiatry.

On Complement Fixation in the Cerebrospinal Fluid of Patients Suffering with Carcinoma.—v. DUNGERN and HALPERN (*Münch. med. Woch.*, 1913, lx, 1923) allude to the fact that inluetics complement fixation may be present in the cerebrospinal fluid, when the blood is negative. Drefus and Almann, indeed, have shown that such may be the case even in the early stages of the infection, when no clinical symptoms are manifest. Since complement fixation may be present in the sera of patients ill with malignant disease when certain antigens are employed, it becomes important to study the cerebrospinal fluid of such patients to determine whether it is capable of binding complement. As antigen, Dungen and Halpern used the acetone extract of the red blood corpuscles of a paralytic and also heart extract. Cerebrospinal fluid was used in amounts of 0.4 to 0.05 c.c. Bloody fluids were discarded. In many of the very cachectic patients it was thought unwise to remove the fluid, so that the number of observations was somewhat limited. The cerebrospinal fluid of 29 patients suffering with various diseases was studied; included in this number were 5 patients with cancer not affecting the central nervous system and a number of syphilitics. The reaction was positive in the cases of cancer, negative in all other diseases examined except lues. By means of the heart extract antigen, it was possible to differentiate the cancerous and luetic fluids, for it was found that the luetic fluids gave positive reactions with both heart extract and blood extract as antigens, while the cancerous fluids were all negative when heart extract was used as antigen but positive with the blood extract.

On the Specificity of the Protective Enzymes (Abwehrfermente).—E. ABDERHALDEN and E. SCHIFF (*Münch. med. Woch.*, 1913, lx, 1923) have examined an immense number of sera from pregnant women and pregnant animals. Whenever the opportunity has presented itself, they have tested for specific enzymes against other organs than the placenta. In 105 cases liver has been tested, in 30 thyroid. With exact technique, they have found the reaction to be specific. Recently, Heilner and Petri have denied the specificity of the reaction. They find that in the case of hematomas all possible organs are digested. Abderhalden and Schiff have studied a number of cases of hematoma. When blood-containing organs were employed, digestion always occurred, but when blood-free organs were substituted, the reaction was always negative. Recently they have found that the serum from a patient suffering from crushing of the muscles and hematoma had no effect on liver or placenta but reacted positively with muscle tissue and blood.

Papaverin as an Aid in the Röntgenologic Differentiation of Spasm and Organic Stenosis of the Pylorus.—G. HOLZKNECHT and M. SGALITZER (*Münch. med. Woch.*, 1913, lx, 1989) refer to the difficulty of determining whether defective gastric motility is due to spasm or to organic stenosis of the pylorus. The duration of the retention is not sufficient; they have observed 2 patients with spasm (proved at operation), where part of the bismuth meal remained in the stomach at the end of twenty-four hours. It has been shown by Pal and others that papaverin diminishes or abolishes the tonus of smooth musculature, both circular and longitudinal. Its effect is much less marked with normal than with pathologically increased tonus. Peristalsis, however, is unaffected. Holzknacht and Sgalitzer have used this drug in connection with their röntgenologic studies of the pylorus. In case pyloric obstruction is found, the examination is repeated, and the second time they administer 0.05 to 0.07 gm. of papaverin hydrochloride *per os* one hour before giving the bismuth meal. In a normal stomach the time of emptying is reduced to one-fourth or one-third the normal. Of 25 stomachs which showed remains of the bismuth meal at the end of six hours, papaverin resulted in lengthening the time in 7, diminishing the time in 6, while there was no changes in 12. Of the 7 cases of the first group (stenosis), 3 have been operated. In only 1 of the second group was an operation performed; here a duodenal ulcer with spasm of the pylorus was found. In those cases where the time of emptying is unaffected, it is believed that spasm and organic stricture co-exist.

Abderhalden's Test in Diseases of the Thyroid Gland.—A. E. LAMPÉ and R. F. FUCHS (*Münch. med. Woch.*, 1913, lx, 2112, 2177) have examined the sera of 60 patients, a few of whom were included in a previous report; all were suffering with disease of the thyroid gland. The sera were tested for specific enzymes according to Abderhalden's method; various organs were used. The material in the present report included 12 cases of Basedow's disease, 11 cases of incomplete or suspected Basedow's disease, 2 of myxedema, and 11 with endemic goitre. Lampé and Fuchs find that the serum of a patient with Basedow's disease always contains an enzyme which is specific for a Basedow thyroid gland and, in a few cases, an enzyme for normal thyroid gland. At the same time there are present in the majority of cases enzymes which attack the thymus and the sexual glands. In the *formes frustes* the same conditions are found. In the sera of two myxedematous patients a specific enzyme for thyroid tissue was also found. Likewise, in endemic goitre the Abderhalden reaction is positive with thyroid gland. The reaction is found to be absolutely a specific one, if the proper care in technique is observed.

Retrohepatic Dulness as a Sign of Typhoid Fever.—In 1911 Lesieur emphasized dulness at the right base as a very convenient and frequent sign of typhoid fever. In the course of the disease, on superficial percussion over the right base of the chest, one can nearly always determine a definite area of dulness, not present on the left, and not explained by pleural or pulmonary lesions. LESIEUR and MARCHAND (*La Presse Méd.*, 1913, p. 625) have sought the sign in 150 patients

under their observation; 114 of these had typhoid fever with positive bacteriologic tests. The retrohepatic dulness was present in 87 (80 per cent.), and absent in 27. Its absence is accounted for by the stage of the disease. It disappears usually toward the approach of convalescence. No one of the negative cases was seen before the twentieth day. In 17 abortive cases the sign was present in 50 per cent. But in no case of any other character was the sign positive. It is uniformly negative in all other infectious diseases. The prognostic value of the sign lies in the fact that its disappearance practically announces the onset of the defervescence. Its reappearance, or its persistence after the fall in temperature is indicative of probable relapse. Lesieur and Marchand believe the sign can be explained by increase in the volume of the liver, due, at least in many cases, to congestion. The variations in the intensity of the sign support this. Lesieur and Marchand hope to determine the pathological explanation more certainly by radioscopy.

SURGERY

UNDER THE CHARGE OF

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Splenic Anemia with Special Reference to Etiology and Surgical Treatment.—RODMAN and WILLARD (*Annals of Surgery*, 1913, lviii, 601), as the result of a study of the literature and experimental work on dogs, say that splenic anemia is a disease entity characterized by a definite symptomatology and pathological picture, and the so-called "Banti's disease" is its terminal stage. In all probability the primary cause of splenic anemia is a toxemia, the origin of which is to be sought for outside the spleen itself, possibly in the gastro-intestinal tract, but the exact nature of which is unknown. This toxin probably acts primarily or secondarily on splenic cells, causing an hypertrophy and increased activity. This increased splenic activity is responsible for the anemia probably through a decreased resistance of the red blood corpuscles. The icteric pigmentation is also due to an increased hemolysis. Although the thrombophlebitis of the splenic and portal veins is a frequent finding, clinically, they believe, from their own experimental work and that of others, that it is not an essential factor in the etiology. If the theory of a primary toxin is correct, they suggest that the blood coming from the spleen to the liver should be doubly toxic in that it contains not only the primary toxin, but that

also elaborated by the splenic substance. To their minds it is the action of this doubly toxic blood that causes the endophlebitis of the splenic and portal veins with consequent thrombosis. In all probability these same toxic factors play the important role in the production of liver cirrhosis, although the mechanical factor of congestion of the portal system may be an additional cause. Up to the present time treatment other than surgical has yielded only temporary benefit. Splenectomy in the first and second stages offers us our only chance of a permanent cure. The mortality is 12.5 per cent. Splenectomy in the third stage will arrest the further development of the disease, but will not cause a retrogression of the liver cirrhosis. In a few isolated cases of early cirrhosis permanent cure has followed removal of the spleen. In the past five years the mortality following splenectomy when done in the third stage has been $56\frac{1}{4}$ per cent. The combination of splenectomy and Talma's operation should be the procedure of choice in this stage.

Nephrostomy: A Permanent or Temporary Means of Delivering all the Urine.—PAKOWSKI (*Jour. d'Urology*, 1913, iv, 373 and 579), quoting Albarram, describes a nephrostomy as an operation for creating a renal cutaneous fistula. This fistula passes through the kidney substance to the pelvis. Pakowski says that all the anastomoses of the ureter to the vagina, the urethra, or the intestine, lead sooner or later to pyelonephritis. Ureterostomy alone can be compared with nephrostomy. It is a more benign operation than nephrostomy. It has the following objections: Drainage is less certain than from the kidney by a nephrostomy, because of the possibility of renal retention from ascending ureteritis or other occlusion and the impossibility of reestablishing the normal course of urine into the bladder or into a new-formed vesical cavity. The objection that can be made to nephrostomy is that it exposes the kidney to the danger of nephritis from time to time or occasionally to the danger of hemorrhage, and on the other hand, it creates a fistula which necessitates the carrying of an apparatus. This last objection applies as much to ureterostomy as to nephrostomy. But the fistula is an inconvenience which can be tolerated. With a good apparatus, and they are numerous, the patients lead perfectly normal lives. They do not carry about a urinous odor. They report the histories of two cases. Both are of men of the world, living a very active life, travelling, hunting, and going about in the world, without any inconvenience. Laying aside the irksomeness of the fistula, nephrostomy presents the following advantages: (1) The opportunity of attacking the renal lesions which made the nephrostomy necessary; (2) the possibility of reestablishing finally the normal course of the urine, if this is considered advisable; and (3) especially the excellent drainage provided by the nephrostomy, drainage which absolutely prevents pyonephrosis and even the reproduction of calculi. The mortality was 4.5 per cent., and in the majority of operated cases, death was due not to the nephrostomy but to the affection calling for the operation. The mortality in all the other methods of operation is greater. The indications for nephrostomy are multiple: (a) In acquired affections of the bladder; malignant tumors, grave tuberculous cystitis, painful and rebellious cystitis. According to the necessity it will be permanent or temporary in (b) congenital affec-

tions of the bladder; exstrophy, absence of sphincter. In these cases it creates for the first time a new reservoir. (c) It is indicated in affections of the pelvic organs which have invaded the bladder or compressed the ureter, such as cancer of the uterus and cancer of the prostate; (d) in traumatic lesions of the bladder or ureter, rebellious vesicovaginal fistula, in particular. (In these cases the nephrostomy opening is maintained only during the repair of the lesions); (e) in certain cases of renal lithiasis, nephrostomy is the only means of preventing the tendency to continuous recurrence of calculi.

One Hundred and Eighteen Cases of Empyema Treated by Operation.—HIRANO (*Deutsch. Zeit. f. Chir.*, 1913, cxxiv, 507) says that while he was not the operator in all these cases, he assisted in all those in which he was not the operator and watched the aftercourse and observed the results in all. One-seventeenth of the cases of empyema developed in adults from serous pleurisy, and two-thirds of those in children. Of the 118 empyemas, 93 were in children from infancy to fifteen years of age. Of 328 cases of pleurisy in adults, 18 were purulent; and of 66 in children, 41 were purulent. Of the 25 cases of serous pleurisy in children, the earliest developed after seven years of age. Of the 118 cases of empyema, 71 were on the right side and 47 on the left side. Hirano saw 2 cases of double empyema in the last two years. In these the empyema developed first on the right side, and after about two weeks on the left side. The majority of his cases were primary, 13 of those in adults and 64 of those in children. Most of the secondary cases in adults developed from serous pleurisy, in children from croupous pneumonia. In 40 per cent. of the cases the pneumococcus was found, in 13 per cent. the staphylococcus and streptococcus. More rarely colon bacilli and pneumobacilli, as well as putrifactive bacilli were found in the pus, but never the tubercle bacilli. In 32 per cent. of the cases no bacteria were found. In only 3 of the bacteria-free cases did animal experimentation show tuberculosis. In many of them the history and symptoms showed probably croupous pneumonia. The period intervening between the beginning of the disease and operation in the adult was: one month in 8 cases, two to five months in 13, and half a year to a year in 4. In children it was: one week in 10 cases, two to three weeks in 30, four to five weeks in 24, six to nine weeks in 23, and ten to thirteen weeks in 6. Six years after complete healing in one child, another empyema developed on the same side and was operated on. The results of operation in the adults were bad. Twelve patients died, a mortality of about 50 per cent. Only 8 cases remained permanently healed. Sixty-seven of the children are still sound (72 per cent.) and 14 have died since the operation (14 per cent.). Of the remaining 5 adults and 12 children, no news was obtained. In the 8 healed adult cases at least half a year was necessary for good cicatrization of the wound. In 4 cases, after resection of one rib, further resection of ribs was necessary. One fourth of the cases in children were healed in three weeks, half of them in four to five weeks, and in the remaining cases six to seven weeks were necessary. Two recovered after two to four months. In his earlier cases Hirano employed gauze drainage, but later used the rubber tube with a gauze strip in the tube.

The Surgical Treatment of Ascites.—SCHWARZMANN (*Deutsch. Zeitsch. f. Chir.*, 1913, cxxiv, 546) reports 14 cases of ascites operated on between 1906 and 1912 and presents a study of the subject. In 2 of his cases (1 and 2) a simple omentopexy was performed. In 4 (4 to 6), the omentum was fixed in a preperitoneal pouch, and in 2 (7 and 8), in a subcutaneous pouch. In 4 (9 to 12), the spleen was fixed in a preperitoneal pouch and an omentopexy was added. In 1 case (13) the left lobe of the liver and omentum were fixed, and in another (14) an omentopexy was done plus a double saphenopexy. The latter operation consists in anastomosing the saphenous vein with the peritoneal cavity. The results of the operations may be summarized as follows: In the first case death occurred 47 days after operation, but no autopsy was done. In the second case (tuberculosis of the abdomen with marked liver cirrhosis), death occurred thirteen months after operation. In the third case there followed a paralysis of the intestines, and autopsy, five days after operation, showed degeneration of the heart muscle. Since there was a severe jaundice and much blood in the stomach and intestines, cholemia must have played an important role. In the fourth case there was tuberculous peritonitis with ascites, and marked liver cirrhosis. The operation was done under local anesthesia and resulted in a much improved condition of the patient. She is still living and fully able to work. In Case 5 there was calcification of the pericardium and heart, mitral insufficiency, and a small cirrhotic liver. The omentum was thickened and already adherent to the parietal peritoneum. No improvement followed the operation. In Case 6 the patient was almost completely bedridden, with marked ascites and tricuspid insufficiency. The operative result was excellent, as she, eight months after operation, is able to do her work and her general condition is very much improved. In Case 7 (alcoholic cirrhosis), the patient died of peritonitis due to a suture deficiency and fistula, from which the ascitic fluid escaped. Case 8 (alcoholic cirrhosis) is completely cured and is one of the best of the cases. It speaks for the subcutaneous fixation of the omentum. Case 9 (alcoholic cirrhosis) became completely able to work and had no more ascites after operation. He died two years after operation from a "heart attack." Case 10 (alcoholic cirrhosis), had severe albuminuria. The peritoneal cavity was drained by gauze. The autopsy showed severe parenchymatous nephritis, calcification of the heart, and beginning pneumonia. In Case 11 an intercurrent hemorrhagic, fibrinous pericarditis, four and one-half months after operation, caused death. Case 12, a girl, aged twenty-three years, had an omentopexy done on her in 1907, for ascites. No improvement followed, and a year later the spleen was fixed subcutaneously with considerable improvement. Case 13 was a confirmed alcoholic, had an aortic, systolic murmur, enlarged heart, and general arteriosclerosis. An omentopexy in a preperitoneal pouch was followed by death three months later. In Case 14 an omentopexy and a double saphenopexy were performed. In the latter operation the saphenous vein was ligated about 8 cm. from its termination and divided distal to the ligature. The proximal stump was then drawn through a small magnesium tube and its margins turned down and fixed over the end of the tube. The intima of the vein was then sutured to the peritoneum.

Sacral Anesthesia in Surgery.—SUCHY (*Deutsch. Zeitsch. f. Chir.*, 1913, cxxv, 1) reports the results of his studies of sacral anesthesia. He says that a new era of sacral anesthesia was inaugurated when Laewen substituted the bicarbonate for the chloride of novokain and obtained a considerably increased effect. His clinical material consisted in 172 cases from Tavel's clinic. Veronal with morphine-scopolamine were employed to obtain preliminary sleep, and proved to be a very serviceable combination. He discusses, among the various phases of the subject, the solutions employed, the technique of its introduction into the sacral canal, and its effects. Of the 172 operations, the anesthesia was a complete success in 106 (61.6 per cent.). In 19 cases (11 per cent.) it was incomplete. These patients complained of mild but bearable pain, so that inhalation anesthesia was dispensed with. In 32 cases (24.3 per cent.), general anesthesia was necessary because of the severity of the pain. In the remaining 15 cases (8.7 per cent.) the sacral anesthesia was a failure. In the main, the women bore the anesthesia better than the men. The associated and after-effects were only transitory, and no persistent troubles were observed. The one fatal termination occurred in the afternoon of the day of operation, from collapse. The autopsy showed the cause of death to be internal hemorrhage, for which the method of anesthesia could not be responsible. The associated symptoms and later disturbances may in the future be reduced to a minimum when a choice of cases is more properly made. Alcoholics with nervous conditions like epilepsy, or with nervous exhaustion, should be excluded. The unequal results will also be improved when the variations in the height of the pelvis are better known and thus cases unsuitable for sacral anesthesia are excluded. These include cases in which the anatomical relations of the sacral canal are such that the trochar is introduced with difficulty and the injection requires strong pressure. The anesthetic fluid employed is a 1 to 1.33 per cent. novokain bicarbonate or phosphate solution with the addition of adrenalin in doses of 40 to 100 e.e. The effect varies in its onset, extent, duration, and intensity. On the average it begins in from eight to ten minutes, and lasts about one to two hours.

Permanent Drainage of Ascites into the Subcutaneous Tissue.—PERINOFF (*Archiv. gén. d. Chir.*, 1913, vii, 1281) discusses the various methods of surgical treatment for ascites. He reports 2 cases in which he employed the method of Maclaire, substituting a silver for a rubber tube. A large semicircular flap was made on the right side of the abdomen, its summit extending inward to the space between the umbilicus and xyphoid cartilage and including the tissues to the aponeurosis. At its base the peritoneum was exposed by a longitudinal incision. A large quantity of fluid escaped. The liver was large and compact and its surface irregular. The omentum was applied at the upper angle of the wound (Talma operation). In the inferior angle a silver tube was introduced into the cavity of the abdomen. This end was shaped like an ordinary catheter, blunt at the extremity with two lateral openings. The other end of the tube was divided into two parts, one curved to each side, which were placed upon the upper surface of the aponeurosis and fixed there by sutures.

The flap was then placed in position and sutured. Primary healing resulted and the sutures were removed in ten days, when a considerable quantity of fluid could be detected under the flap. In the first case before operation the circumference of the abdomen was 112 cm., and there was considerable asthma. In the last ten days of the twenty-nine days in the hospital after operation, the circumference of the abdomen varied between 95 and 98 cm., and the asthma had disappeared. In the second case before operation the circumference of the abdomen was 106 cm., and a month after operation it was 86 cm. The general condition of both patients was much improved by the operation. Perinoff concludes that the Drummond-Talma operation imitates nature by forming a supplementary circle of circulation. Unfortunately the beneficial results of this operation are not manifested immediately and the patient often perishes before they can do so. Permanent drainage into the subcutaneous tissue should be added to give an immediate effect. When the supplementary circulation is formed the drainage can be done away because it then becomes useless.

Cholera and Typhus Gangrene, Symmetrical Gangrene in the Balkan War without Danger from Frost.—WELCKER (*Zentralbl. f. Chir.*, 1913, xl, 1625) saw 115 cases of the above type of gangrene among the Bulgarian soldiers. Almost without exception, seven to fourteen days before the development of the gangrene, the patients had passed through an attack of cholera, or had suffered from dysentery or diarrhea (80 per cent. had cholera and 20 per cent. dysentery or diarrhea). These conditions did not precede the gangrene in 14 cases. The gangrene began during convalescence or somewhat earlier, generally two to three weeks after the beginning of the typhus. With rare exceptions, the cause of the gangrene can be found in some disease, and when this fails it is probable that the history is faulty. Welcker does not agree with Wieting and others that cold and wet are important factors in the causation of the gangrene. Wieting studied the same cases on the Turkish side in the same war. After the cholera had been suppressed by the Bulgarians and only rare cases developed, the characteristics of the cholera gangrene disappeared and only the typhus gangrene remained.

THERAPEUTICS

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Progress in Antityphoid Vaccination during 1912.—RUSSELL (*Jour. Amer. Med. Assoc.*, 1913, lxi, 666) gives some interesting tables and charts that show very well the results of antityphoid vaccination

as applied in the U. S. Army. He says that during the past four years over 200,000 persons, mostly in the military or naval services, have been immunized without any fatalities or untoward results. There have been no reports of cases indicating that the vaccination has activated latent tuberculosis or any other disease; in fact, as regards tuberculosis, there has actually been a diminution in the number of cases of all classes of tuberculosis during this period. He makes it a rule to vaccinate the healthy only, and any febrile illness, whatever its nature, automatically postpones vaccination. It is due perhaps to this precaution that there has been freedom from bad results in the use of typhoid vaccine in the army. The practice of antityphoid vaccination has been a pronounced success in the military and naval services, in hospitals, schools, institutions and in the camps of pleasure seekers and contractors; in fact, wherever in military and civil life it has been used. He feels that its more general use, especially among the young, is advisable. The fact that it occasionally fails to confer complete protection is not a valid objection to its use, but rather an indication for its repetition at intervals to be determined in the future. A practiced program is easily formulated on the following basis: No prophylactic vaccination is needed by persons living in a city or country district in which the typhoid rate is continuously low. If, however, a person, young or adult, leaves such a region for one in which the typhoid rate is high or the changes of exposure greater than at home, vaccination is indicated. It is, of course, indicated in cities or country districts with high typhoid morbidity. Revaccinations may be managed after the plan used in vaccination against smallpox, that is, in childhood, youth, and again when exposure threatens.

Indications for the Treatment of Pulmonary Disease by Rest and by Exercise.—KUHN (*Beiträge zur klin. d. Tuberculose*, 1913, xxvii, 311) believes that the lung in cases of pulmonary tuberculosis should be kept either entirely at rest or expanding actively. He says that conditions between these two extremes favor the growth of the tubercle bacilli. The lung may be kept absolutely at rest by inducing pneumothorax. The indications for this plan of treatment are extensive processes, especially those with cavity formation and in all those cases where the temperature cannot be kept normal under the usual plans of treatment. On the other hand cases which do not have fever should be treated by cautious breathing exercises so that the lung capacity may be increased. The exercise treatment is contra-indicated in the presence of large cavities, in the acute secondary infections, and in all cases with a persistent temperature. He believes that the best method for exercising the lung is the aspiration mask devised by him. He gives a number of illustrations which show the symmetrical enlargement of the chest and expansion of the lung that resulted from the systematic use of his aspiration mask. The use of the aspiration mask may be so graduated that the forced breathing is carefully regulated and under constant control.

The Action of Salvarsan on the Kidneys, Especially after Mercurial Administration.—LOEWY and WECHSELMANN (*Berlin klin. Woch.*, 1913, I, 1342) relate their experiments on dogs that, according to them,

indicate that salvarsan has an injurious action upon the kidneys, especially if they are previously damaged by the administration of mercury. This injurious action was most marked upon the water-eliminating function of the kidney and in some of the dogs complete anuria followed the injection of salvarsan. Furthermore, it was found that the urine might remain free of albumin to the end, and it is therefore apparent that the albumin test is unreliable as an indication of the toxic action of salvarsan upon the kidneys. Therefore they emphasize the importance of carefully observing the water metabolism after the administration of salvarsan for therapeutic purposes. The experiments indicate further that the danger of administering salvarsan is increased when the kidneys are not previously sound or after systemic mercurial treatment. Consequently Loewy and Wechselsmann warn against the practice of a combined mercury and salvarsan course of treatment.

Effect of Diuretic Drugs on Life of Animals with Severe Acute Nephritis.—WALKER and DAWSON (*Arch. Int. Med.*, 1913, xii, 177) relate their experimental work as to the effect of certain diuretics upon the life of animals having acute nephritis produced by uranium nitrate. From their experiments they conclude that the diuretic drugs, theocin, caffeine and potassium acetate definitely shorten the life of a rabbit having a severe acute experimental nephritis produced by uranium nitrate. Theocin and potassium acetate gave quite parallel results and were slightly more harmful than caffeine. Spartein sulphate, although not nearly so detrimental as the other drugs, however, did, in some cases, shorten the animal's life. Water in large amounts is detrimental in some cases, possibly depending on the severity of the nephritis. The diuretics alone in large doses, and water alone in large doses, when given intravenously to normal animals for a reasonable length of time, do not shorten their life and probably are not toxic in themselves. They believe that diuretics are probably contra-indicated in severe acute nephritis in man, since in animals in such cases they shorten life.

Clinical Results with Digipan.—WEISS (*Munch. med. Woch.*, 1913, lx, 2499) writes concerning digipan, a preparation derived from digitalis which contains digitoxin and digitalin in practically the same proportions as they are present in the plant itself, while the irritating digitonine is practically eliminated in the process of manufacture. This preparation is recommended as a very satisfactory remedy for clinical use. With relatively small doses and in a short time the desired clinical effects such as increased blood pressure, slowing of the pulse, and diuretic action are obtained. Digipan may be given by mouth, in liquid or tablet form, or injected intravenously or intramuscularly. No untoward by-effects and no evidences of cumulative action were observed after the administration of digipan.

The Treatment of Pneumonia with Partially Autolyzed Pneumococci.—ROSENOW and HEKTOEN (*Jour. Amer. Med. Assoc.*, 1913, lxi, 2203) have found that when virulent pneumococci are suspended in normal salt solution the substances on which their resistance to phagocytosis

and virulence depends pass into solution. The soluble part at a certain stage of autolysis is highly toxic and has little immunizing action, while the insoluble remnants have well-marked antigenic properties and practically no toxic effects. The protective value against experimental pneumococcus infections of detoxicated pneumococci has been found to be greater than that of heat-killed pneumococci. The details of preparing the antigens or vaccines are given in the article. The injections were given subcutaneously every day in doses of 10,000,000,000 to 20,000,000,000, until the temperature reached normal. Only slight tenderness followed the injection and there was little local or general reaction noticeable. The cases treated are divided into three classes: the cases treated outside of hospital practice, the uncontrolled cases in the hospital, and those controlled by alternate untreated cases. Of 30 cases occurring in the practice of physicians outside the hospital, 3 died. Of 35 cases in the second group, 9 died, a death rate of 25 per cent. The third group comprised the greatest number treated. The type of pneumonia in this group has been the worst, comprising a considerable number of alcoholics. Every second pneumonia patient in the order admitted to the hospital during January, February, and March of 1911, 1912, and 1913 received subcutaneous injections of detoxicated pneumococci. With this exception the treatment did not vary from that of the control group. There were 294 cases for consideration in this group, 146 receiving the treatment and 148 constituting the controls. Of the control group, 56 died, a death rate of 37.8 per cent., while of the injected group 34 died, a death rate of 23.3 per cent. Rosenow and Hektoen believe that, in view of the fact that the mortality was consistently lower in the injected cases of each year, that the average time of the first injection was late (approximately the fifth day) and that the type of cases treated was of the worst kind, the conclusion that this method of treatment of pneumonia is of value seems warranted. The results obtained in the series outside of the hospital, in which the injections were begun earlier, indicate that by the early administration of the antigen better results can be secured.

The Results with the Röntgen Treatment of Tuberculous Cervical Adenitis.—FEITSCH (*Münch. med. Woch.*, 1913, lx, 2610) has had good results with the use of the Röntgen ray treatment in tuberculous adenitis of the cervical lymph nodes. This treatment has been used in 33 cases of whom 8 are entirely cured and 8 are much improved. The details of the technique of administering the treatment are given in the article. The length of treatment averages six months. In some of his cases the effect of the treatment was a marked reduction in the size of the lymph nodes involved, leaving a hard lump which was easily removed under local anesthesia. This, as Fritsch emphasizes, is a distinct advantage in that it obviates the necessity of operating with general anesthesia in cases with pulmonary involvement.

The Autoserosalvarsan Treatment of Syphilis of the Central Nervous System.—McCASKEY (*Jour. Amer. Med. Assoc.*, 1914, lxii, 187), following the technique of Swift and Ellis has given twenty intraspinal injections of neosalvarsanized serum to 7 patients with various forms

of syphilis of the central nervous system. He says that remarkable improvement resulted in some cases and believes that this method of treatment, with perfect asepsis and cautious dosage, is devoid of danger, and offers a new and entirely rational method of attack on the localized infection in cases of cerebrospinal syphilis.

PEDIATRICS

UNDER THE CHARGE OF

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Addison's Disease in a Boy, with Calcification of the Adrenals.—H. D. ROLLESTON AND E. J. BOYD (*British Jour. Child. Dis.*, 1914, xi, 105) report a case of Addison's disease in a boy, aged twelve years. A general bronzing of the skin developed gradually. It was especially marked around the nipples, the umbilicus, and pudenda. There were a number of pigmented scars on the body but no buccal pigmentation. The boy developed synchronously loss of energy, drowsiness, a cough at night and nocturnal enuresis. An uncle and a brother are said to have had tuberculosis. There were no signs of pulmonary or spinal tuberculosis and von Pirquet's reaction was negative on two occasions. The spleen and liver were not palpable. There was no valvular disease of the heart nor any dulness behind the sternum. The skiagraph showed calcification in the adrenal glands and discrete and dense opacities at the hila of the lungs suggesting calcified nodules. The red-cell count was high, 6,492,000, and there was a high lymphocyte count supposed to be indicative of lymphatism, and a bad prognosis. The eosinophiles were high, from 5 to 7 per cent. The size of the heart was small.

The Child in the Tuberculous Milieu.—MAURICE FISLABERG (*Archiv. Pediatrics*, xxxi, 96) details a study of all the children of tuberculous applicants for relief to the United Hebrew Charities in New York City during three months. The social and hygienic condition of these children was investigated and all the children under fifteen years of age were examined medically and the cutaneous tuberculin test applied. The children were re-examined in four months and the tuberculin test again applied where the first was negative. There was at least one tuberculous member in each of the 217 families investigated. The hygienic conditions offered all the predisposing factors to the spread of the disease—poverty, congestion, lack of fresh air and sunshine, underfeeding, and an abundance of tuberculous sputum near at hand. Of the 692 children aged under fifteen years, 92 per cent. were exclusively breast fed. However, it seems that as long as the child remains in the tuberculous milieu it is immaterial whether it is breast fed or not, as it is bound to become infected either way.

These children were found short of weight as compared with children of non-tuberculous parents. Enlarged thoracic veins seem to be a fair sign of compression of the main trunks by enlarged glands or adherent pleura. Among the 692 children 67 per cent. had swollen cervical glands. These were for the most part non-tubercular. Enlarged tonsils and adenoids were found in 58.6 per cent. Fislberg agrees with Simon that these hyperplasias have nothing in common with scrofula and tuberculosis. The external stigmata of tuberculosis such as tuberculides, phlyctenula, etc., were exceedingly rare in this series. The tuberculin test was applied to all the children, using crude or concentrated tuberculin and the von Pirquet method. Of the 692 children, 465, or 67.25 per cent. gave a positive reaction. The proportion of positive reactions during the first year was 15 per cent., at two years, 55 per cent., increasing steadily to 74.5 per cent. during the eleventh to the fourteenth year, and reached 83.79 per cent., counting the 37 children at fourteen years alone. Of the 692 cases, 65 showed symptoms and signs of active tuberculosis.

Etiology of Intestinal Catarrh in Infants.—KARL BAERTHLEIN and WALTER HUWALD (*Deutsch. med. Woch.*, 1914, xl, 418) investigated the flora of the intestinal tract in infants to determine the type of bacteria present in health and in diseased conditions of the bowel. The three classes of cases examined were (1) infants with intestinal diseases only; (2) as controls, infants with pneumonia, meningitis, hydrocephalus, syphilis, and diphtheria; and (3) 100 healthy infants. The average age was from a few days to one year. The cultures were made from material taken from the bowel by means of sterile glass tubes. The investigation was made during the summer and continued to December. Out of 72 cases of primary intestinal affections, 21 showed bacteria belonging to the dysentery group, 7 showed paratyphoid-B bacilli, and 12 showed the *Bacillus pyocyaneus*. Among the 72 cases the feces in 40, or 55.5 per cent. showed pathogenic bacteria. Among the control cases suffering from other diseases and among the healthy cases, but 1 case in a healthy child, showed bacilli of the dysentery group. The colon bacillus was found in 38.5 per cent. of the intestinal cases, 26 per cent. of those otherwise ill, and 12 per cent. of the healthy cases. *Bacillus proteus* was found in 21 per cent., 34 per cent., and 6 per cent. of the cases respectively. Organisms similar to the paratyphoid-B bacillus appeared in 13 per cent., 2 per cent., and 14 per cent. of the cases respectively. The 21 cases of intestinal disease showing bacilli of the dysentery group were the most severe, in their clinical symptoms, of the whole group, and 11 of the 21 died. In a number of cases the dysentery bacillus was found after death in the spleen and gall-bladder.

The Occurrence of Apical Tuberculosis in Children.—ERICH SHIKA (*Wien. klin. Woch.*, 1914, xxvii, 173) sketches first the adult type of tuberculosis which in the majority of cases begins in the apex of the lung. He recalls the insidious onset of the disease, the anorexia, gradual loss of weight and strength, the changes in the lung almost imperceptible at first, then gradually developing frankly into the physical signs of an apical tuberculosis. By a natural comparison the same

general symptoms in children are taken to mean apical tuberculosis by many physicians and faint or imagined changes in the percussion note or breath sounds at the apices in a child with pallor, anorexia, and poorly nourished body, are sufficient evidences to make a diagnosis of apical tuberculosis. But since the Röntgen ray has been utilized in the diagnosis of pulmonary conditions the difference between the diagnosis, clinically made and the actual condition in the lung, has become manifest, and it has been shown that most of the diagnoses of apical tuberculosis are wrong. Shika here differentiates between the apex of the lung and the upper lobe, which latter may be the seat of a tubercular process. But upper lobe tuberculosis is not a beginning condition in children, it is a terminal condition, almost always associated with the severe constitutional symptoms of a "tuberculously old" child. In six years of x -ray work devoted exclusively to children. Shika has found but three cases of apical tuberculosis. These were all in older children of twelve or thirteen years. Errors of diagnosis usually came under two groups: (1) cases in which the x -ray showed normal lungs and normal skeletal development of the thorax; (2) cases which showed changes in the lung or the thorax or in both. The majority of Shika's cases of wrong diagnosis fall in the first group, showing normal lungs and thorax. The type of child in which most frequently the erroneous diagnosis of apical tuberculosis is made, is that in which occurs rapid growth in length, slow growth in width, poor muscular development generally, thereby giving to the thorax the long and narrow appearance which is identified in the adult as the *habitus phthisicus*. The pallor in this type of child is a pseudo-anemia and due to abnormal blood distribution. The irritability of the nervous system is characteristic and the physical resistance is naturally poor. Bronchial catarrh is frequent, and the elevation of temperature in the evening so often seen is really due to muscular or nervous fatigue. On all these signs the erroneous diagnosis is most frequently made, while the x -ray shows almost always that the lungs are sound.

Epidemic of Dysentery in Little Children.—E. KEUPER (*Münch. med. Woch.*, 1914, lxi, 474) discusses dysentery in general and reports an epidemic of this disease. Epidemics of dysentery in adults have been frequently reported in which the organism was of the so-called Y-type and of the Flexner type, grouped under the term *Bacillus pseudodysentericus*. Pseudodysentery is less severe than the real dysentery, and often occurs sporadically. There have been very few epidemics of this disease reported as occurring in children. A number of investigators have only found the pseudodysenteric bacillus in those cases in which the stools showed pus and blood. Keuper reports an epidemic of 20 cases in children from a few months to five years old. The usual severe symptoms of rapid loss of weight, frequent stools containing mucous and blood and great prostration prevailed. All showed a trace of albumin and cylindroids. Six of the children died, 4 of them being under ten months old, and succumbing to hyperpyrexia and convulsions. One case died of an intercurrent pneumonia, and one case, aged five years, died from sarcoma. The *Bacillus pseudodysentericus* was found in the greater majority of cases. The incubation

period was not more than five or six days. Out of the 6 deaths, 2 showed at postmortem no pathological changes in the intestinal tract. The other form showed anatomically only a relatively mild follicular enteritis, which would indicate that this disease is almost always a dysentery. After convalescence two negative tests of the feces are not sufficient to prove the cases non-infectious, as the bacilli may remain in the bowel for months, and rigid isolation for a long time is often necessary. Relapse occurred in 5 of the 20 cases, and lasted from two to six days. In 2 of these relapsed cases and in 2 other cases, the bacillus was found in the stools two months after the illness.

OBSTETRICS

UNDER THE CHARGE OF

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Thrombosis and Embolism in the Puerperal Period.—JUNGE (*Archiv f. Gynäkologie*, 1912, Band xcvi, Heft 2) contributes an interesting paper upon this subject and has collected an extensive series of statistics. His study of the subject leads him to believe that alterations or injuries to the endothelium of the bloodvessels producing interruption of the circulation is the most important factor in causing thrombosis. Such lesions are present in 26 per cent. of all labors, but do not develop sufficient severity to cause the complications in question. Multiparæ at middle life are most apt to have this lesion, and it occurs in them in 71 per cent. Puerperal thrombosis in some form develops in 74 per cent. of multiparæ, and of these 72 per cent. are cases of varices. In the first days of the puerperal period the saphenous vein is most often affected; in the latter portion of the puerperal period the femoral; and in the midportion of the puerperal period the pelvic veins. The lesion is bilateral very frequently, but when the saphenous vein is affected it is usually upon the right side, the femoral vein upon the left. This accident happens after obstetric operations, hemorrhage, infection, systemic disease, and prolonged labor, and especially in multiparæ who have varicose veins before labor. One attack predisposes to a second. The process begins with very slight elevation of temperature. The highest fever is seen when the femoral vein is involved, but no premonitory symptom can be definitely recognized. Thrombosis of the saphenous vein gives a good prognosis, while the same complication in the deeper veins is much more serious, as it predisposes to pulmonary embolism. He reports 81 cases from Fehling's clinic in Strassburg, and gives condensed histories of 22 of especial severity. Fortunately, embolism is comparatively rare, for in the records of 10,056 labors in the Strassburg clinic there were 81 cases of thrombosis, and but 4 cases of embolism—0.04 per cent.—with but one fatal issue.

When the records of other clinics are compared in 16,000 labors in the Dresden clinic there were 20 cases of embolism, or 0.0125, with 14 fatalities. This is the largest number in his collection of statistics, other clinics giving an average closely resembling the Strassburg clinic.

DUFFEK (*Archiv f. Gynäkologie*, 1912, Band xcvi, Heft 2) contributes a paper upon septic thrombosis, reporting a series of experiments upon animals. He finds that in the human subject septic thrombi show a peculiar formation resembling coral, which readily produces detached masses forming emboli. These are composed of leukocytes and layers of fibrin and contain bacteria, while the permanent masses are not so rich in germs. The formation of a thrombus and the localization of bacteria indicate that the activity of the bacteria has become limited to the local lesion. Under normal conditions the uterine veins at the placental site very rarely form detached masses. In puerperal infection these thrombi become infected and later become separated. Where the uterus is in a tonic condition and is not in active contraction, whether in pregnancy or the puerperal period, the separation of thrombi from their original site rarely occurs. The question as to whether there is a premonitory symptom of thrombosis and embolism has occasioned considerable discussion.

KÜSTER (*Zentralblatt f. Gynäkologie*, 1911, No. 30) has maintained that there is no premonitory alteration of pulse and temperature in cases of thrombosis or embolism.

MICHAELIS (*Zeitschrift f. Geburtshilfe und Gynäkologie*, 1912, Band lxx, Heft 1), maintains his original contention that the pulse and temperature are always altered before thrombosis and embolism occur. In this connection it may be well to recall Machler's sign, that the pulse rises out of proportion to the temperature, the temperature often falling after a preliminary rise, while the frequency of the pulse steadily increases. The effort to lessen puerperal mortality is a constant one and meets with varying success.

In view of the recent discussion upon midwives in America, Grünbaum's paper (*Zentralblatt f. Gynäkologie*, 1912, No. 35) is of interest. He believes that midwives should conduct cases of labor without internal examinations. In 1000 confinements, 741 were conducted without an internal examination, while 259 were examined. This would indicate that 75 per cent. of cases do not require internal examination. It is usually thought that the omission of examination is dangerous because abnormal presentations and prolapse of the cord will not receive early recognition. In the 1000 labors there were 5 transverse positions which were recognized by external examination only. There were 7 cases of prolapse of the cord, in 3 of which the patient was brought into the clinic with the cord pulseless. In the remaining 4 diagnosis was made easy three times sufficiently early to save the child. In but one case could omission of internal examination be blamed for the loss of the infant. When one comes to study the influence of internal examination upon morbidity, it is found that among those not examined the general morbidity was 2.1 per cent., and of these but 0.6 per cent. were from puerperal causes. Among those examined the morbidity was 6.6 per cent. The general mortality of this entire series of cases was 0.3 per cent., and there was no death from puerperal septic infection. Among these patients 95 were operated

upon, of whom but 5 had a moderate elevation of temperature. This occurred among 37 forceps cases and 14 versions. In 3 transperitoneal Cesarean sections, one had abscess in the abdominal wall.

GYNECOLOGY

UNDER THE CHARGE OF

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New Operation for Rectal Prolapse.—SIPPEL (*Zentralbl. f. Gyn.*, 1914, xxxviii, 297) describes an operative procedure which he devised for the treatment of a rectal prolapse in a patient aged sixty-eight years. The prolapsed portion of the rectum formed a mass outside the anus, about the size of a small fist, and was composed entirely of the pelvic portion of the rectum and lower end of the sigmoid, the anal portion of the rectum for a distance of about 3 cm. above the sphincter remaining in place, the pelvic portion prolapsing through this and through the sphincter. The perineum was somewhat relaxed, but the uterus was forward, in good position, and showed no tendency to come down. The first step in the operation was to make a longitudinal incision through the entire posterior wall of the vagina and cervix, exposing the anterior wall of the rectum from the sphincter to the reflection of the peritoneum at the bottom of Douglas' pouch. The peritoneum was pushed upward somewhat, and the lateral flaps of the posterior vaginal wall, with the underlying tissue, were dissected well back on each side, so as to give a good exposure of the greatly distended and relaxed anterior wall of the rectum. This was then infolded in a longitudinal direction by transversely placed sutures, the process being repeated four or five times, until practically the whole anterior wall was folded into the lumen in the form of a thick, longitudinal ridge, the diameter of the rectum being reduced by this means about to normal size. The upper portion of the rectum was then firmly sutured to the posterior surface of the cervix, these sutures serving at the same time to close the incision in the latter. An anterior colporrhaphy was performed; the redundant portions of the flaps of the posterior vaginal wall were cut away, and the edges brought together with deeply placed sutures, which included in their bite a portion of the rectal wall. The separated levator fibers were then brought together, the rectal wall being included in these sutures also. The operation was concluded by a plication of the sphincter, which was quite markedly relaxed. In this manner, the portion of the rectum which showed a tendency to prolapse was firmly anchored to the cervix, the posterior vaginal wall, and the levator ani. The wounds healed well, and the patient shows after six months every appearance of being permanently cured. Sippel suggests that in similar cases, in which, however, there is some tendency to prolapse of the uterus, a firm ventrofixation of this organ to the anterior abdominal wall might be necessary in addition.

Bacteriology of Leucorrheal Discharges.—A praiseworthy attempt has been made by CURTIS (*Surg., Gyn., and Obst.*, 1914, xviii, 299) to throw some light on a subject upon which we possess very little definite knowledge—the bacterial flora of the lower female genital tract under normal and pathological conditions and the relation of bacteria to the production of leucorrhea. Although the paper represents merely a preliminary study, which has not as yet led to definite results, several points are presented of considerable interest. As a result of his studies, Curtis has come to the rather surprising conclusion that purulent discharges rarely come from the uterus or cervix, arising practically in all cases in the lower genital tract, since in a number of instances cultures taken from the endometrium and cervix failed to show the presence of any bacteria. The typical discharge for which, in his opinion, the cervix is responsible is mucus, which forms in the vagina an excellent culture media for any organism which may come in contact with it. In all, 75 patients were studied, 35 of these suffering from a profuse leucorrhea. The material for culture was taken from various portions of the vagina, chiefly the vicinity of the cervix, and was inoculated on blood-agar, blood-ascites-agar, and other media, and grown under aerobic and anaerobic conditions. Fresh smears were also examined, and were found to contain a preponderance of the large, Gram-positive “vaginal bacilli” of Döderlein; in normal cases these being practically the only organisms present. In purulent discharges, however, there are always enormous numbers of other varieties of organisms, among which Gram-negative bacilli tend to predominate. By far the greater number of organisms present in such discharges are anaerobic in nature. In cultures made from the vulvar region, however, the relative number of aerobes is much greater than in those from the upper portions of the vagina, the chief organisms in the former region being *B. coli*, staphylococci, and pseudodiphtheria bacilli. Several animals were injected with washings and fresh material from the four worst cases of leucorrhea in the series, without any distinct evidence of toxicity being discovered. A considerable number of bacilli and cocci, showing various cultural characteristics, were isolated, but most of these have not been definitely identified. Streptococci were almost never found in fresh preparations, but were seen to develop from diplococci on artificial media. They cannot, therefore, be considered of any considerable importance in the production of leucorrhea, nor can the colon bacillus; while the preponderating role is apparently played by the anaerobic group; the gonococcus is, of course, by far the most important single organism. In a surprisingly large number of cases, however, this eventually disappears so completely that it is not demonstrable by any method at our command, which suggests that perhaps the chief role played by it is in preparing the soil for the leucorrhea-producing anaerobes. Curtis states that apparently some practical results from this work will be obtained, in the form of vaccine therapy, but that he is not prepared to report upon this phase of the subject as yet.

Regeneration of Endometrium after Curettage.—Some interesting histological studies of the exact manner in which the endometrium regenerates after the uterus has been curetted have been undertaken

by RICHTER (*Gyn. Rundschau*, 1914, viii, 47). He performed a curettement at varying periods before operation upon a number of uteri, whose removal was necessary on account of some condition, such as chronic adnexal disease, which did not greatly affect the endometrium, and also carried out a series of experiments upon dogs. He found that by the end of the first twenty-four hours the fresh wound caused by the curette is covered with a layer of fibrin and polymorphonuclear leukocytes, an expression of an inflammatory reaction to the injury on the part of the tissue. During the next twenty-four hours the picture remains practically the same, except that the leukocytes increase in number. After the third day, however, the picture varies somewhat according to whether the traumatism has been deep or superficial. In the deeper wound areas young bloodvessels, accompanied by leukocytes and fibroblasts, begin to grow into the fibrin layer, the fibroblasts apparently arising not from the remnants of old endometrium, but from the connective tissue which lies between the muscle fibers of the uterine wall. The epithelial covering, however, is supplied always by a gradual extension over the surface of the newly formed connective tissue of cells from some neighboring island of preserved mucosa, or from the fundus of a gland that has escaped destruction, the epithelial covering being practically complete by the ninth day. Gradually a fibrous intercellular substance is formed, especially in the deeper portions of the new endometrium, the superficial layers remaining more distinctly cellular. Up to as long as the twenty-sixth day, however (beyond which the investigations did not go), this tissue is wholly without glands, the only indications of these being a few shallow depressions in the surface epithelium, from which it is possible, but not definitely demonstrated, that new glands may be developed by ingrowth. Such development would therefore be centripetal in direction; it certainly takes place slowly, if at all. The more superficial wounds, on the other hand, are covered in large areas by epithelium as early as the third day, and by the fifth the process of epithelialization is complete. The stroma formation is analogous to that seen in the deep wounds, but gland regeneration occurs certainly in a centrifugal direction, from undestroyed ends of glands lying between the muscle fibers. This process is fairly rapid, for in these areas the gland regeneration is practically complete by the fifth day. In deep wounds, where some of the muscle tissue is removed, as often occurs when curettage is vigorously performed, this appears never to regenerate, but to be replaced by connective tissue.

OTOLOGY

UNDER THE CHARGE OF

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Examination into the Hearing Power, Comparatively, of Blind Persons and Persons with Average Normal Vision.—HORTER

(Passow's *Beiträge*, 1913, vi) made tests as to the audible duration of the tuning forks in the Bezold-Edelmann series in the two classes of cases the result proving that the blind have no special compensatory accentuation of the sense of hearing and that improvement in the hearing proper does not accrue with duration of the loss of sight; in other words, that there is no evidence of educative improvement of the function itself. On the other hand, the blind appear to listen and to hear more concentratedly than do seeing persons and are less disturbed in their effort at hearing by surrounding, concomitant, conditions. From Horter's observations it would seem to be evident that while the actual hearing power is not augmented in the blind it is a far more effective means of determination of the direction of a sound source and of its progress in motion, constituting, therefore, for the blind, the most important sense for a determination of the relationship of the environment; this is true not only of rhythmic recognizable sounds but of the incoördinated sounds constituting noise. Under these circumstances it is the duty of the medical profession and of the schools both to take measures to conserve and to educate a sense which is of so much importance to the ambulant ability of the blind, it being made a stated part of the curriculum of the blind to train the exercise of the hearing power for purpose of orientation and also to compensate for the possible want of acute hearing by education in acuity of attention and of observation.

Otitic Migraine.—MARGULIES (*Prüger med. Woch.*, 1913, No. 27) reports 4 cases of migraine with vertiginous attacks during which there was a general, and considerable, depreciation in the hearing, this depreciation lessening with recovery from the vertigo and the hearing being normal in the period between attacks. The explanation of Barany as to the conjectural cause of the symptom complex which bears his name is not accepted by Margulies as applicable to the cases which he has observed and made the subject of his paper; in his opinion the cause was neither adhesions nor cyst formation but merely an increased exudate due to some irritation which subsided and decreased as the irritation decreased, with a corresponding disappearance of the symptoms, the point of attack being presumably labyrinthine. In all probability the labyrinth and vestibular apparatus play a larger rôle than has heretofore been supposed in the causation of migraine, and although labyrinthine symptoms such as are evidenced in these reported cases are rare the frequent observance of hyperesthesia acustica as an accompaniment of migraine may be justifiably taken as concurrent evidence.

Primary and Secondary Suture in Mastoid Operations.—WALB (*Zeitschr. f. Ohrenheilkunde*, 1913, lxviii) recommends preferentially the primary suture, as he has practised it for twenty years both in the typical mastoidectomy and in the radical operation, leaving the lower end of the wound free and open, without even a gauze drainage wick and removing the subcutaneous continuous wire suture at the end of eight days. In only a small percentage of the cases was the wound left open, unsutured, and then in deference to the presence of an uncovered and possibly not normal sinus or the complication of an extradural abscess when it was desirable to keep the wound cavity

open for inspection. Even in these cases, if the suppurative process had terminated and the wound had become aseptic eight days or more after the operation he made a secondary suture in the same manner as that primarily practised. The tamponage used in the non-sutured cases was not too firmly pressed and was more lightly made as the cases progressed toward recovery.

Aural Diagnosis of Constitutional Syphilis.—BECK (*Münch. med. Woch.*, No. 50, 2778) was able to demonstrate, in a considerable number of cases of syphilis with normal hearing, and in other cases of the same class in which there had never been indication of aural disturbance, a marked depreciation of the hearing by bone conduction this symptom being present in 80 per cent. of the syphilitics examined and tested for hearing by bone conduction. Similar clinical observations and tests having been heretofore made, with like results, in instances of intracranial processes accompanied by encroachment upon the lumen of the cranial cavity, brain tumors for instance, in other cases also in which there was no indications of aural participation and in cases of hydrocephalus, all accompanied by a considerable degree of intracranial pressure, it seemed possible that the occurrence of this symptom is syphilis might be explained in the same manner. In order to arrive at a definite conclusion lumbar puncture was done in a series ofluetie cases exhibiting the symptom of decreased duration of hearing by bone conduction. A repetition of the tests a few hours after the lumbar puncture showed that the symptom had disappeared, to return, however, in from two to three days. The relationship between increased intracranial pressure and the shortening of duration of hearing by bone conduction was confirmed by the examination of patients with only the initial symptoms of sclerosis, negative Wassermann, and absence of localized swelling of the lymphatics. In the primary stage this symptom was, with very few exceptions, absent, it was most frequent in those cases in which the infection had become constitutional and the general systemic evidences appeared. As the result of these observations Beck is of the opinion that in the case of an otherwise apparently healthy patient without other aural symptoms but with a definitely decreased duration of hearing by bone conduction the question of a possibleluetie cause should be considered.

Facial Paralysis in Fractures of the Petrous Process of the Temporal Bone.—DE STELLA (*Archiv. Internat.*, xxxv, 3), in the cases of fracture of the base of the skull and of the petrous bone, found that two types were distinguishable. The first and less frequent occurred at the moment of the injury and resulted from an implication of the bony wall of the nerviduct of the facial to such an extent as to directly wound the nerve or to result in its compression by hemorrhagic exudate. Recovery was established, unless the nerve had been actually divided, in from six to twelve weeks. In the second more usual type the paralysis appeared not immediately but from two to four days after the injury, originating presumably in a secondary compression of the nerve as the result of an inflammatory exudate about and within the nerve, a condition almost inevitably incident to a basal fracture either with or without extension to the nerviduct of the facial. The duration of the

paralysis, to the time of recovery is, in this class of cases, usually short. In the case of the first type mentioned there was an interesting complication in a concurrent paralysis of the abduceus resulting from pressure exercised by a hemorrhage at the apex of the petrous bone in the line of the fracture.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Resistance of the Intestines to Gastric Digestion.—MARIE and VILLANDRÉ (*Jour. de Physiol. et de Path. générale*, May 15, 1913, xv, No. 3) have continued their experiments bearing upon whether or not intestine in contact with gastric juices is digested. The open jejunal loop with its mucosa exposed was found by them, to remain for months without any trace of digestion, if its blood supply were not damaged. The close jejunal loop had equally good fortune under the same circumstances, and Marie and Villandre consider that interference with the vascular supply is the essential feature of this type of necrosis. They think further that the greatest enemy to proper blood supply is not muscular contraction, but rather the way in which sutures are placed, especially considering that there is danger to the graft by infection through the bacteria in the stomach contents attacking the points of suture. The gastric juice is able to play only a secondary part in the disappearance of the closed loop, that is, it is able only to finish destruction already begun by a necrosis of vascular or inflammatory origin; in other words, it can digest only dead tissue. These experimental facts are entirely contrary to Katzenstein's theory of a specific antipepsin in the stomach and duodenal walls; he considered the causation of ulcers as dependent upon differences of equilibrium between the pepsin and antipepsin. The living intestine, Marie and Villandre say, if well nourished is as far removed from the danger of digestion as the stomach wall itself, and they point out that in addition the spleen, gall-bladder, and omentum, if their vitality be not too seriously injured by intervention, are equally capable of making an effective resistance to the gastric juice. Claude Bernard's theory of epithelial protection to explain the resistance of the stomach is also contradicted by Marie and Villandre's experiments in which they exposed an intestinal serosa and, again, a naked muscularis to the gastric juices; these, like the mucosa, were also able to resist. The gastric epithelium tends to cover by proliferation the foreign body, provided it has not already a mucosa. To consider the defence as due to mucus coating the surface of the foreign body, it is hardly probable that it can efficaciously cover the large grafted surfaces if these are not themselves provided with mucus-bearing cells.

The Endotoxin of the Bacillus Typhosus.—BARANTCHIK (*Rousski Vrach*, xii, 289, 1913) has used Kravkoff's method of extracting from bouillon cultures of *B. typhosus* a substance which appears to belong to the nucleoproteins, and proves to have an extremely toxic action. Intravenous injection of the same kills the rabbit in doses of 0.02 grams per kilogram; subcutaneous or peritoneal injections are less fatal. The symptoms and pathological changes observed after an acute intoxication by this substance correspond in all particulars to those which may be observed in animals infected by the living culture. In the blood appear the specific antibodies for the bacillus, and the agglutinins, precipitins, and bacteriolysins, are similarly specific, and we must recognize in this substance a specific endotoxin which preserves all the peculiar features of the antigen of *B. typhosus*. Considering with this that antitoxic substances do not exist in the blood of the cured cases, or in the animals immunized by the living bacilli, Barantchik concludes that the bacillus produces no ectotoxin.

Effects of Anesthetics in Nephritis.—MACNIDER (*Jour. Med. Research*, August, 1913, xxviii, No. 3) gives the results of his observations upon anesthetics in animals who are already the subjects of nephritis from the use of uranium. In the kidney damaged by this means the epithelial injury is greater than that of the vascular system, although both are observable, and adult and old animals are more susceptible to these changes than young animals. The use of an anesthetic increases the severity of the changes which were found, and this again proves to be of greater extent in the old than in the young. MacNider lays stress once more upon the peculiar differences which are manifested by different parts of the tubules in reaction to the irritation, the proximal parts of the tubules being least affected, while the loops of Henle showed more pronounced lesion. Contrary to what one might expect MacNider found that morphine-ether anesthetic was less toxic to animals who were the subjects of such nephritis, than the chloroform-alcohol combination.

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All communications should be addressed to—

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THE
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ORIGINAL ARTICLES

SARCOMA OF THE STOMACH.

BY CHARLES H. FRAZIER, M.D.,

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THE stomach is one of the most unusual sites for sarcoma. The infrequency of the lesion, and the recovery of health following an extensive resection of the stomach prompt me to place my experience with a single case on record. The first case of primary sarcoma of the stomach was recorded by Bruch, in 1847, in his *Diagnose der bösartigen Geschwulste*; in 1864, Virchow referred to 3 cases, while as late as 1893 Tilger was able to collect only 20 cases. From this time on additional cases have been placed on record, and recently G. Flebbe, in an exhaustive treatise on the subject, chiefly from the pathological view-point, assembled 157 cases, the larger number of which, however, were discovered at autopsy. In the following statistics, sarcoma of the stomach appears to be a rather unusual lesion. Yates found in 800 stomach tumors only 2 per cent. were sarcoma; Drost and Wild in 423 sarcomas of various structures mention but one of the stomach. Of 840 sarcomas at the Berlin Pathological Institute there is only 1 of the stomach. Tilger mentions 4 in 3500 sarcomas. In 23 consecutive cases of primary malignant disease of the stomach, Fenwick found 2 sarcomas, Hosch 6 in 13,387 autopsies; Czerny saw 2 in 298 gastro-enterostomies, while Haberkant in 207 resections of the pylorus met with 3. Thus it may be said that of primary malignant disease of the stomach, sarcoma is represented in only 2 per cent., that only 0.25 per cent. of all sarcomas are found in the stomach, and only 0.045 per cent. of all cases coming to autopsy.

On December 20, 1912, I saw on my service at the Episcopal Hospital, a woman (M. F., No. 4299), aged thirty-six years, whose chief complaint was vomiting and heart-burn. She had been subject to light attacks of indigestion for the past twelve years, which were promptly relieved by the remedies prescribed by her physician. The patient dates the onset of her present trouble to January, 1912, about twelve months ago, when she began to have vomiting spells accompanied with nausea or pain, coming on suddenly and without warning, usually about three hours after eating, at first two or three times a week, lately more frequently. She had never vomited any blood; had never been jaundiced, and had lost twelve pounds in twelve months. There was nothing in her family history or in her previous personal history of note save that she had had typhoid fever and smallpox. Upon examination she appeared considerably undernourished; there was a moderate pallor of the skin, but nothing unusual about the condition of the thoracic and abdominal organs other than the lesion about to be described.

Upon inspection of the abdomen, the outline of a mass about the size of a pear could be readily seen, extending across the left hypochondrium, about two inches above the umbilicus and an inch to the right of the midline. The mass rose and fell with respiration, and when grasped could be moved freely in all directions. It was firm in consistency and irregular on the surface. I was somewhat in doubt as to the source and nature of the mass. Its mobility reminded one of that of a floating kidney, although it did not appear to be in the retroperitoneal space, and its shape did not conform to that of the kidney. To determine its relation to the stomach, I percussed the abdomen before and after a draught of two tumblerfuls of water and realized at once that the tumor was in close relation with the pyloric portion of the stomach. The findings at this examination, taken with the history of vomiting, and the positive evidence of retention, determined subsequently by the raisin test, led me to make a provisional diagnosis of a scirrhus carcinoma. The history of an indigestion for over twelve years was suggestive of an ulcer period, the existence of which as a forerunner of carcinoma was not lost sight of.

The patient readily consented to an operation, which I performed December 24, 1912. Through a high right rectus incision the abdomen was opened and the tumor exposed; it involved about a third of the greater curvature, and was nearer the pylorus than the cardia. Attached to the lower margin of the growth were two loops of jejunum. The lymph nodes along the greater and lesser curvatures and about the celiac axis were considerably enlarged.

Although it seemed more than probable that the metastasis had extended beyond the first lymph-node station, and the chances of a radical cure thereby lessened, the increasing obstructive symptoms and consequent inanition justified the removal of the growth

if only for palliative purposes. I proceeded, therefore, with the operation and rescted with the growth about two-fifths of the stomach. In addition a portion of the two adherent loops of the jejunum had to be excised. The operation was concluded with a posterior gastrojejunostomy and the rent in the mesocolon attached to the line of suture. The operation was bloodless, the convalescence uneventful, and the patient was discharged on the ninth day. Only recently, that is, in November, 1913, ten months after the operation, I received from the patient a letter to the effect that she was perfectly well and had regained her normal weight.

Both prior to operation and when the tumor was exposed on the operating table, I was under the impression that we were dealing with a carcinoma implanted on an ulcer base. The specimen was sent to the laboratory, and the following report revealed to my surprise that we were dealing with a lymphosarcoma:

PATHOLOGICAL REPORT.—(Dr. C. Y. White). Lymphosarcoma of the stomach; metastatic lymphosarcoma of the serous coat of the adherent loops of jejunum. The specimen, representing a considerable portion of the stomach with the tumor, is about six inches long, two inches wide, and three-quarters of an inch thick.

Mucosa: The glandular tissue of the mucosa has for the greater part been replaced by cellular infiltration. When the remaining ducts are present, they are widely separated by the infiltrating cells. Extending from the mucosa through the submucosa, the infiltrating cells form a dense layer, which is responsible to a great extent for the increased thickness of the stomach wall. In the muscular layers are to be found wide and narrow tracts of cellular infiltration. These are prominent enough to be seen plainly with the naked eye in the stained specimen.

The histology of the nodule on the serous coat of the jejunum showed a nodule of whitish color fairly firm and about the size of a walnut. Section shows the nodule to be composed of fatty tissue, fibrous tissue, and a dense cellular collection. These latter cells compose about nine-tenths of the tissue.

General consideration of the type of infiltrating cell: The cells found in the stomach wall are chiefly of the small and medium sized lymphatic type. There are, however, in the less densely packed areas, cells of larger type with a moderately large vesicular nucleus and considerable protoplasm. The majority of the cells show surrounding protoplasm. In a few areas these cells are densely packed, suggesting lymph nodes. Mitotic cells are fairly numerous throughout the section. The same type of cell is found in the nodule removed from the jejunum; here, however, they are far more numerous and very densely packed, and mitotic cells are numerous. The bloodvessels throughout the section of the stomach and the metastatic nodule are thin walled and by no means numerous. A connective-tissue frame work throughout both sections is not at all prominent and represented by thin bands.

A SERIES OF TWENTY-EIGHT OPERATIVE CASES ARRANGED IN CHRONOLOGICAL ORDER, WITH STATISTICAL DATA.

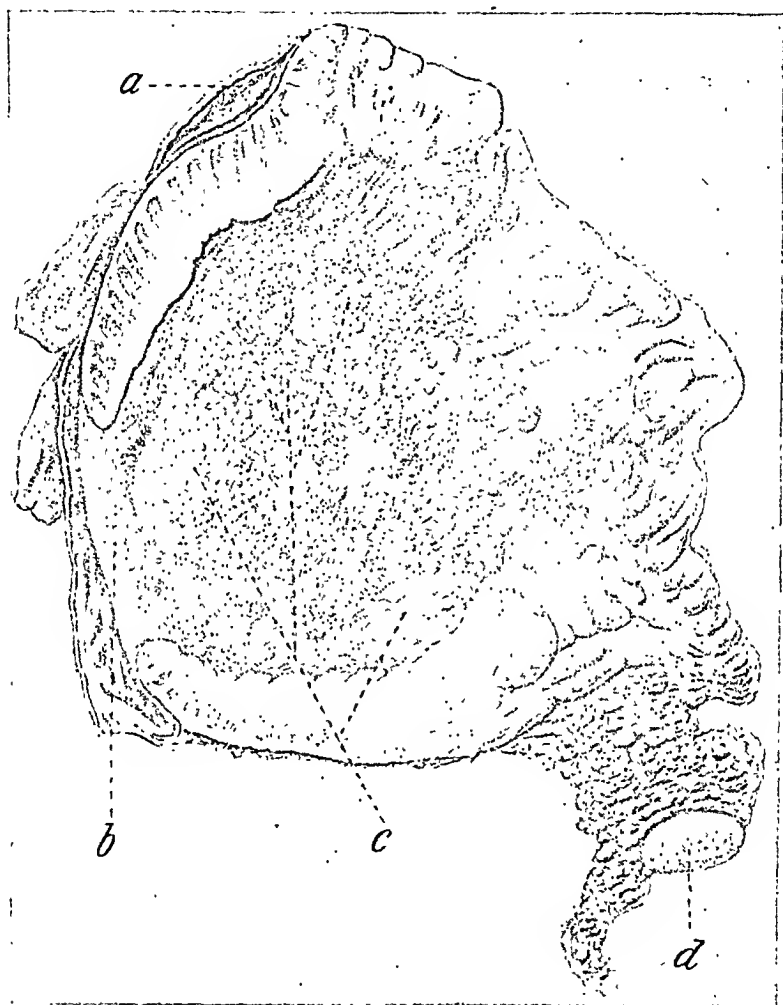
Author.	Date.	Sex.	Age.	Variety.	Site.	Metastasis.	Results.
Billoth	1888			Round-celled	Anterior wall	Successfully removed.
Torók (Salamán)	1892	F.	21	Round-celled	Successfully removed.
Hartley	1896	F.	54	Spindle-celled	Posterior wall	Successfully removed.
Morton	1899	M.	39	Round-celled	Diffuse	Duodenum	Removed. Well after two years.
Cantwell	1899	F.	52	Spindle-celled	Posterior wall	Successfully removed.
Finlayson	1899	M.	3½	Mixed-celled	Posterior wall	Recurrence eight months later.
Capello	1899	F.	54	Cystic	Well two years after.
Dock	1900	M.	55	Lymphosarcoma	Successfully removed.
Schöph	1899	F.	60	Lymphosarcoma	Well after one year.
Herman	1901	F.	60	Myxosarcoma	Greater curvature	Successfully removed.
Midodowski	1903	F.	40	Large round-celled	Posterior wall	Operation; death.
Bird	1903	M.	41	Mixed-celled	Pylorus	Duodenum	Recurrence three years after.
Moser	1903	F.	17	Myosarcoma	Lesser curvature	Operation; death.
Moser	1903	F.	41	Myosarcoma	Posterior wall	Pancreas	Successfully removed.
Moser	1903	M.	50	Myosarcoma	Posterior wall	Adrenal	Death.
Alessandri (Salamán)	1903	F.	53	Fibromyoma	Greater curvature	Successfully removed.
MacCormick-Welsh	1906	F.	53	Spindle-celled fibrosarcoma	Posterior wall	Well five months later.
MacCormick-Welsh	1906	M.	62	Large spindle-celled	Posterior wall	Well two months later.
Yates	1906	R.	57	Large round-celled	Posterior wall	Successfully removed.
v. Eiselsberg	1906	M.	44	Fibrosarcoma	Fundus	Successfully removed.
Yates	1906	F.	58	Spindle-celled	Posterior wall	Well four and one-half months later.
Moschcowitz	1909	F.	58	Spindle-celled	Greater curvature, near cardia	Death.
Maryland and Anderson	1910	F.	57	Spindle-celled	Greater curvature	Recovery
Rupert	1912	F.	58	Lymphosarcoma	Diffuse	Gastrectomy, 1898. Well fourteen and one-half years after.
Moschcowitz	1912	M.	50	Lymphosarcoma	Pylorus	Well nine months later.
Kondring	1913	F.	35	Spindle-celled	Greater curvature	Recovery.
Ameling	1913	M.	5	Myosarcoma	Pylorus	Well nine months after.
Sudder	1913	M.	29	Spindle-celled	Posterior wall	None	Well eleven months after.
Frazier	1912	F.	36	Lymphosarcoma	Greater curvature	Jejunum lymph nodes	Well nine months after.

Pathologically the tumor conformed to one of the two types most commonly represented in sarcomas of the stomach. While all forms of sarcoma may be found, the small round- and spindle-celled types predominate. In an analysis of 61 cases, I found 23 spindle-celled, 16 small-round celled, 3 large round-celled, 6 lympho-sarcoma, 7 myo-sarcoma, 5 myxo-sarcoma, and 1 cystic sarcoma. In conformance, too, with the general rule, the specimen which I removed originated in the pyloric portion of the stomach, the common seat of small round-celled variety in contrast to the spindle-celled, which usually involves the fundus and chiefly the posterior wall. The spindle-celled variety is slower in growth, slower in metastasizing, more apt to be circumscribed, often becoming pedunculated, forming a round, hard, movable mass in which ulceration is rare and late. It usually springs from the submucosa and dissects its way between the mucous and muscular coats. Although more frequently found near the pylorus the round-celled does not only actually occlude its lumen, but by infiltrating the stomach wall renders it rigid and the pylorus patulous. The expulsive power of the antrum is crippled by the extensive infiltration of the muscularis, and for this reason symptoms of obstruction and retention, conspicuously represented in my own case, are often found (see illustration). The widespread and diffuse infiltration of the round-celled variety is not unlike the lesion found in lymphocythemia, and when similar lesions are found in other organs, the process in the stomach should be regarded as an expression of lymphocythemia rather than as a primary malignant growth. The round-celled type rarely gives a palpable tumor, is more rapid in its course with earlier metastasis and well-marked cachexia.

As to the most frequent sites of the tumor, some reference has already been made. Flebbe mentions 37 cases where the pylorus was reported involved, the greater curvature in 30, the posterior wall in 26, 13 on the lesser curvature, the anterior wall in 8, the cardia in 3, in 2 the pylorus and both curvatures, while in 27 cases almost the entire stomach was infiltrated.

Contrary to the belief that sarcoma is most frequently found in the young and in early adult life, an analysis of recorded cases shows that sarcoma of the stomach is more frequent in later adult life; in 35 cases collected by MacCormick and Welsh, 11 occurred between fifty and sixty years, 6 between forty and fifty, 6 between sixty and eighty, while there were but four between twenty and forty years. The youngest was three and a half years, while the oldest was eighty-five years. These results are comparable with those of Corner and Fairbanks, who found the incidence greatest between the ages of forty and fifty years. In a recent review in 17 cases by Scudder, in which the author makes the statement that gastric sarcoma is a disease of the young, 14 occurred in people over forty, while only 3 were under this age.

As with most of the unusual forms of tumors or common types of tumors in unusual sites, the true nature of the lesion is not revealed until the histological examination has been made. In the case reported, I was reasonably confident we were dealing with a carcinoma, and there was no means either of proving or disproving this preliminary diagnosis before the abdomen was opened and the



Lymphosarcoma of the stomach. The specimen represents a portion of the stomach removed for lymphosarcoma. *a*, portion of the intestine adherent to the tumor and resected; *b*, the pylorus; *c*, the seat of the tumor; *d*, lymph nodes.

specimen examined. As a matter of fact, I have been unable to find a single instance where the true nature of the lesion was known prior to operation or autopsy. The difficulties are illustrated by the case of Köndring, in a female, aged thirty-five years, who had had gastric trouble for eight months. Upon examination a fluctuating tumor was found filling the entire lower abdomen to a

hand's breadth above the umbilicus. It was thought to be a cystic ovary, but the operation revealed a primary cystic spindle-celled sarcoma springing from the posterior surface of the greater curvature near the fundus. In general terms, it may be said that given a patient presenting gastric symptoms of several months' duration, with a readily palpable, freely movable tumor of the stomach, but without the loss of weight, general debility, and cachexia common to carcinoma of the same duration, one might be justified in suspecting sarcoma.

The expectation of life varies with the duration of the lesion prior to operation and the character of the tumor. In the 28 cases tabulated in the appended table the end results are recorded in but few. The period of survival was mentioned in but 12 of these; 1 had survived fourteen years, 2 two years, 1 one year, 1 had recurrence in three years, and 8 were reported as well from two to eleven months after the operation. Naturally as elsewhere, although seemingly much later in the course of the growth, metastasis takes place. Secondary growths have attacked the mesentery, omentum, colon, small intestine, peritoneum, pancreas, abdominal wall, kidneys, pleura, lungs, ovaries, scrotum, bone, and skin. Howard found metastasis in 40 per cent. of cases, in 50 per cent. along the lymph channels, Lofaro in 50 of 123 cases, and Hoesch in 39 of 85 cases. As metastasis takes place relatively late when compared with cancer, the size of the tumor and its duration should not deter the surgeon from resecting as much of the stomach as need be when this can be accomplished without undue risk.

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CRITICAL EXAMINATION OF ONE HUNDRED PAINTERS FOR EVIDENCES OF LEAD POISONING.

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AT the request of Dr. Alice Hamilton, of the United States Department of Commerce and Labor, I undertook the examination of 100 able-bodied painters, based upon (1) complete family, personal, and occupational history, (2) chief symptomatic and industrial complaints, (3) physical examination, and (4) certain significant tests, with the view of establishing the prevalence of plumbism or its after-effects among them. The source of material was from a large Chicago painters' union, whose officials for some years past had been giving considerable attention to morbidity and mortality statistics among their members.

These workmen may be said to constitute the highest type of such tradesmen to be found in Chicago as regards intelligence, industry and thrift, trade application, morality, personal hygiene, and general interest in personal and community welfare. A large percentage were of foreign extraction, rearing, and trade apprenticeship. According to the statements of these, they had used very little lead paint before coming to America, zinc being the principal foreign substitute.

The examinations were made in the six weeks' period between February 22 and April 4, 1913. By an arrangement with the men

and their officials the candidates came at stated hours to the examiner's office. Each case required about one hour's time, the examination of blood-smears and the analysis of the urine for lead being completed outside of this time. It may be stated that these examinations were made at the end of the winter's slack season, consequently all the men examined should have exhibited the minimal immediate effects of plumbism. The men were not taken from a sick list, but from those who attended the weekly meetings or were present at the business headquarters of the union.

CASE HISTORIES.

AGE.

Between 20 and 25 years	7 men.
Between 26 and 30 years	14 "
Between 31 and 40 years	26 "
Between 41 and 50 years	33 "
Between 51 and 60 years	17 "
Over 60 years (62, 67, 68)	3 "
Total	100 "

PARTICULAR TRADE PROCESSES.

General painters, many doing some paperhanging	63 men.
Interior painters and decorators, some paperhanging	32 "
Exterior painters exclusively	2 "
Carriage painter exclusively	1 "
Paperhangers, doing some painting	2 "
Total	100

NATIONALITIES.

Scandinavian born	51 men.
German born	9 "
American born	20 "
Hebrews (mostly foreign born)	9 "
Miscellaneous foreign born	11 "
Total	100 "

TIME AT TRADE.

Two men had begun the trade at the ages of thirty and thirty-one. (With these exceptions all had begun as youths).

Less than 5 years at the trade	1 man.
Between 5 and 10 years at the trade	17 men.
Between 11 and 20 years at the trade	32 "
Between 21 and 30 years at the trade	28 "
Between 31 and 40 years at the trade	17 "
Between 41 and 50 years at the trade	4 "
For 54 years at the trade	1 man.
Total	100 men.

BEGAN THE TRADE.

United States of America	48 men.
Abroad	41 "
Not ascertained	11 "
Total	100 "

Father's Occupation that of Painting in 15 cases.

Significant Family History. The age of parents, cause of death, father's occupation, number of brothers and sisters, with cause of and age at death, were inquired into in all cases. While allowing for the unreliability of laymen's statements, still the following was deduced concerning parents, brothers, and sisters;

Tuberculosis	100 inquiries, 8 positive, 4 questionable
Cancer	75 " 9 "
Insanity and epilepsy	70 " 5 " 2 questionable

Significant Personal History.

No previous diseases (other than venereal and not including probable instances of lead poisoning) 53 cases.

Suggestive evidence of plumbism in the past based upon:

(a) Physician's diagnosis	10 "
(b) Paralyzes: both wrists	1 "
both legs	1 "
(c) Appendicitis (1 questionable)	2 "
(d) Encephalopathy (epileptiform seizures, delirium or unconsciousness without fever or other diseases than probable plumbism) (2 others questionable and 1 further, which was undoubtedly due to methyl alcohol.)	3 "
(e) The "lead triad" (abdominal colic, obstinate constipation, severe headache without fever, with or without vomiting, all of these coming in "spells" or attacks lasting a couple of days or more and without other assignable cause) (2 others questionable.)	32 "
(f) "Rheumatism" (as lumbago, sciatica, pleurodynia, brachialgia, etc.), excluding cases of rheumatic fever, nerve traumatism, etc.	51 "
(g) Statements as to previous existence of lead-line in gums were discarded as unreliable.	
(h) Negative evidence of any of the above conditions	27 "
(i) Positive evidence of one or more of the above conditions	73 "
Serious accidents	24 "
Serious operations (2 appendicitis, 4 hernia)	6 "

Serious diseases:

Typhoid	18 "
Pneumonia	11 "
Malaria	11 "
Pleurisy	8 "
Infections (2 smallpox)	3 "
Inflammatory rheumatism	4 "
Tuberculosis (1 questionable)	3 "
Bronchitis	2 "
Nephritis	1 "
Multiple lipomata	1 "
Wood-alcohol blindness (partial in 2 cases, recovery complete in 1 case)	3 "
Jaundice	1 "

Venereal diseases:

Not ascertained	10 "
Denied	49 "
Gonorrhea	32 "
Chaneroids	9 "
Syphilis (3 others questionable)	4 "

Habits. The approximate extent of the consumption of beverages, etc., was inquired into by ascertaining the number of cups or "drinks" per day. None admitted the use of habit-producing drugs, and there was no evidence of same. In the following table

the term "moderate" has the following applications: in the case of tea or coffee, the use of not over four cups per day; in the case of beer, not over three glasses per day; in the case of whisky, not over two "drinks" per day.

Beverage.	None.	Occasional.	Moderate.	Excessive.
Tea	41	27	32	0
Coffee	7	7	73	13
Beer	10	34	42	14
Whiskey	22	52	20	6

I believe that these figures are fairly accurate, also that the tendency to moderation among the 100 men examined is rather better than for the average tradesmen.

Marital History.

Single (always)	24 men.
Married or widowers	76 "
Married one year or more	74 "
Wives never pregnant	11 "
Pregnancies but no living progeny	10 "
With living progeny	53 "
Statistics on miscarriages, no certain information.	
Association between wives washing leaded garments and miscarriages, no certain information.	

Progeny.

1 child living	14 men.
2 children living	18 "
3 " "	12 "
4 " "	5 "
5 " "	2 "
6 " "	2 "
8 " "	2 "
Total living children of 74 men, married at least 1 year	144
Average " " 74 " " 1 "	1.95

Progeny and Age of Married Men. There were 49 married men of forty years of age or over, of whom 37 had living progeny.

There were 35 married men of forty-five years of age or over, of whom 26 had living progeny, whereas 7 had had none at all. In this group 2 had a total of 28 children with 16 living. The total progeny of the group was 116 children, or an average of 3.31 each; total living progeny was 75 children, or an average of 2.14 each; this includes the two large families, without whose statistics the respective averages would be 2.67 and 1.79 each. This is certainly very low for married men of at least forty-five years of age. Analysis showed that these same 35 men with their total of 116 living and dead progeny came from families having a total of 235 offsprings. While this group of forty-five-year-old painters may have more progeny, it is not likely they will double the same, as would be necessary to equal their own ancestral average.

Just what part lead poisoning and what part various social conditions may have had to do with this decreased progeny is impossible of ascertainment.

COMPLAINTS.

(a) *Hygienic Complaints and Comments.*

Breathing lead paint dust from sandpapering	99 cases.
(Inquiry showed the men would have no objection to substituting zinc for lead)	
Sickened by turpentine in close quarters	64 "
Sickened by benzine in close quarters	70 "
Sickened by "hard-oiling," practically all cases.	

The men complain most bitterly of the effects of "hard-oiling" upon sensorium, skin, and digestive tract; less so of turpentine upon the digestive tract, sensorium, and bladder; and least of benzine upon sensorium, occasionally upon the digestive tract.

Wood alcohol has been largely displaced by denatured alcohol, according to their statements. Few men claim that they use either to any particular extent. Those who had been blinded had been performing special work, as in brewery vats, etc.

Other frequent complaints, particularly of respiratory, skin, and stomach disturbances, were: varnish removers, ammonia and lyes, fusel oil, oxalic acid, muriatic acid, acetone, amyl-acetate, creosote, naphtha, and various patented "dope" varnish-and-paint removers.

Time at noon hour: This was invariably one-half hour, although many stated that by special arrangements with their employer one hour might be had, providing an extra half-hour were added at the end of the day. Many said they would prefer this, as the half-hour noon-time was insufficient for properly washing up, eating, etc. *Working day* was eight hours (8 A.M., to 12 noon; 12.30 to 4.30 P.M.).

Washing of hands before eating: All the men questioned claimed a knowledge of the danger of lead poisoning from paint on hands. All stated they endeavored to wash hands with soap and water where possible; occasionally one carried his own soap and towels; most resorted to benzine to remove the paint, while a number claimed that they always ate their sandwiches, pie, etc., held in pieces of paper. Few gave much attention to the lips.

Mustaches: Fifty inquiries showed that these were worn constantly in 18 cases, occasionally in 7 cases, and not at all in 25 cases. Beards were not encountered. Only a few men had considered deposition of paint and dust in mustaches and the possibility of straining drinks through same as dangerous. Some considered that they protected nasal breathing; this is certainly a wrong impression.

(b) *Present Health Complaints:* The following list of symptoms, embracing those most commonly occurring in acute or chronic plumbism, was inquired into in the case of each of the 100 men. They may be considered as the complaints of the past few weeks or months:

Symptoms.	Severe.	Moderate.	Slight or occasional.	Total.
Loss of strength	12	4	16
Loss of weight	9	3	12
"Nervousness"	5	19	9	33
Digestive:				
Nausea	1	14	1	16
Anorexia (morning)	3	13	8	24
Foul taste	4	17	12	33
Foul breath	2	7 (?)	?	9 s.c.
Salivary disturbances	2	16	?	18 s.c.
Emesis	6	4	10
Constipation	15	19	16	50
Diarrhea	2	8	9	19
Melenæ	2	3	5
Hemorrhoids	5	13	10	28
Visceralgia	9	18	16	43
Colic	4	3	7
Distention	8	18	9	35
Sensorial:				
Headache	17	14	19	50
Vertigo	4	19	13	36
Syncope	2	4	6
Insomnia	4	6	12	22
Nightmare	1	5	5	11
Depression	1	3	4	8
Confusion	6	2	8
Memory failing	s.c.	14	7	22
Neuromuscular:				
Neuralgia	1	3	2	6
Arthritic pains	3	10	11	24
Anesthesia and paresthesia, especially of arms	2	18	6	26
"Rheumatism"	1	18	16	35
Muscular cramps	1	12	11	24
Trembling	2	7	8	17
Ocular (especially "spots" and diplopia)	6	17	7	30
Itching eyelids	1	8	5	14
Aural (tinnitus, deafness)	4	23	13	40
Urinary (incontinence, nocturnal frequency)	7	27	4	38
Genital (impotence)	1	3	3	7
Circulatory (palpitation, epistaxis)	12	15	27
Festering cuts	1	1	2
Neurasthenic	1	5	9	15

Special symptoms associated with severe or acute plumbism, such as psychoses, paralyses, paroxysms, aphonia, etc., were not encountered.

Comments on the Above Table. So far as possible, specific causes of any of the above symptoms, other than lead poisoning, have led to the exclusion of such symptoms in the above table, that is, (1) in cases of rupture, visceralgia, constipation, and distention were omitted; (2) neuralgias due probably to teeth were omitted; (3) joint pains and "rheumatism," due to acute inflammatory rheumatism, past or present, were omitted; (4) defective vision, due to refractive errors, omitted as far as possible; (5) aural disturbances, due to otitis media, omitted so far as possible; (6) urinary disturbances were in nearly all cases due to nocturnal frequency, not to venereal diseases, and rarely to incontinence; most cases occurred in those of advancing years; only one due to diabetes.

PHYSICAL FINDINGS.

The following scheme was carried out in each of 100 cases, with abnormal findings as listed:

General:	Cases.	Remarks.
Appearances unhealthy	10	
Pallor	7	Not marked in any.
Emaciation, general	4	Not marked in any.
Emaciation, local (arms)	5	Not sought for in but 25 instances.
Prematurely aged	8	
Loss of expression	1	
Loose teeth	18	
Lead line	19	10 not pronounced.
Pyorrhea	51	Pronounced in 17.
Tremor, lips or tongue	27	
Tremor of hands	19	
Deafness	4	All rather pronounced.
Nystagmus	4	
Mydriasis	12	
Myosis	2	
Unequal pupils	4	
Argyl-Robertson pupil	2	Neither with absent knee-jerks.
Ptoxis	1	
Strabismus	4	All since early childhood.
Conjunctivitis	4	Rather marked in one.
Atrophic nails	1	
Wrist tumor (no injuries)	2	1 ganglion, 1 small bone; no typical Gubler tumor.
Pulse-rate	5	All arrhythmias.
Pulse-tension	See blood-pressure below.
Arteriosclerosis (radial)	11	
Incoördination (arms)	17	1 well marked, 6 moderate, 10 slight.
Wrist reflexes	4	2 absent, 2 markedly increased.
Wrist paralyses	0	
Chest:		
Heart abnormal	23	Including 2 questionables.
Lungs abnormal	20	7 emphysema, 1 acute bronchitis, no pronounced tubercular lesions, although 14 were suspicious.
Mediastinum	1	Dulness with tenderness.
Abdomen:		
Enlarged liver	6	
Hernia	6	
Distention (gaseous)	7	Including 1 hernia, 1 ascites.
Superficial tenderness	0	
Deep tenderness	2	1 gall-bladder?
Operation scars	8	4 hernia, 2 appendix, 2 genital.
Abdominal reflex absent	12	
Genitalia:		
Hydrocele	2	
Undescended testicle	1	
Cremasteric reflex absent	26	
Retraction of testes	7	
Skin:		
Dryness	2	1 ichthyosis.
Dermatitis	6	Mostly wrists.
Aene	6	
Dermographia	1	Very marked.
Extremities:		
Gouty toe-joint	8	
Edema of ankles	7	6 with varicose veins.
Epitrochlear glands	2	Out of 50 examinations.
Knee-jerks abnormal	16	3 absent, 13 exaggerated.

SPECIAL TESTS.

1. *Sodium Sulphide Skin Application.* This was made in 90 cases, using a 5 per cent. solution by means of an applicator. The test usually shows positive on the hands, wrists and forearms of any who have worked in lead, particularly painters, within a week or ten days, that is, a brown or black streak resulting immediately after the application. In all of my cases the hands and arms had been washed with soap and water, in many cases for a period of over several days, since the workman's last exposure to lead paint or dust. It appears that the oil and turpentine in the paint, as well as benzine used by the men to cleanse the skin, cause the paint to infiltrate the deeper layers of the epidermis and probably the follicles and skin glands to such an extent that the normal slow exfoliation is necessary to remove it. DuMoulin's test,¹ although based upon an incorrect assumption as to its value, is an amplification of this means of proving the presence of lead. Of course, other black sulphides, as copper, mercury, bismuth, nickel, and cobalt, had to be ruled out, but usually none of these concern painters. The test demonstrates to the painter himself in a very striking manner the extent to which he is actually encased in a sheet of lead, despite his soap-and-water ablutions. Out of 62 men who reported they had worked at least an hour or more with lead paint or its dust within the previous two weeks, this test was positive on hands, wrists, and forearms in 42 instances. Continuing the applicator up the arm and down the chest to the umbilicus, 6 were positive all the way; in other words, such men were practically entirely encased in a sheet of lead buried deep in the skin. I will not attempt to enter into the discussion as to the probability of absorption from this source.

2: *Urinary Analysis.* The cursory analysis was made from a fresh specimen in each case. In addition, most of the men, in response to a special request, brought a pint bottle of urine, which, being added to that part of the fresh specimen not required for immediate tests, gave several hundred cubic centimeters for the determination of the presence of lead. Of course, twenty-four-hour specimens would have been more satisfactory, and on this account the urinary features of contracted kidneys had to be omitted. Specific gravity, color, turbidity, and reaction were first determined in each sample. Albumin was sought for by the heat and acetic acid tests and by Heller's test. Reducing bodies, by Haines' reagent, supplemented by Nylander's test when indicated. Indican by Obermayer's and Lavelle's methods preceded by the lead subacetate preparation. In the remaining urine, lead

¹ Bull. de l'académie royale de Médecine de Belgique, 1884, p. 1093.

was sought for in 39 cases, selected as being the most promising although in all of these more urine should have been taken.

I am indebted to Dr. F. M. Meixner for the lead analyses, which were made with special equipment in the laboratory of the Cook County Hospital. Briefly stated, possible lead combinations in the urine were decomposed by adding to the specimen about one-tenth its bulk of pure nitric acid, boiling down to 60 c.c., filtering, washing residue, and the total filtrate of about 90 c.c. subjected to electrolysis in a properly covered lead-free beaker. By means of three dry cells arranged in series, connected up with a miniature rheostat, and a double-pole switch, a current of two volts at a milliampèreage of about 4 was maintained for a period of 8 hours in the solution, using platinum electrodes coiled in spiral form. The beaker was kept at 37° to 40° C. by an electric bulb. A browning or blackening of the electrode attached to the carbon pole gave presumptive evidence of lead, deposited as the peroxide, which was determined quantitatively by comparing the weight of the dried electrode before and after the electrolysis, also by colorimetry, and qualitatively by the usual methods. Three control experiments to determine delicacy of the method showed:

Dilution.	Percentage recoverable		
	Experiment 1.	Experiment 2.	Experiment 3.
1 to 100	99.8	99.7	96.0
1 to 500	99.4	99.7	96.8
1 to 1,000	99.7	99.4	97.3
1 to 5,000	95.2	92.0	90.0
1 to 10,000 (blackening of electrode but weights and therefore percentages not determined).			

The above results were obtained by using the required amount of lead salt to make the dilution in 500 c.c. water.

The more significant results of the urinary analysis in brief were as follows:

Acid reaction (usually sharp)	95 cases.
Albumin plus casts	7 "
Dextrose	1 "
Indian found to be increased	19 "
" " excessive	8 "
Lead present (0.16 and 0.11 mg.) traces (?) in some others	2 "

3. *Blood Examination.* (a) A blood-smear was made in each case and afterward stained by Harlow's solution.² These were examined for evidence of blood dyscrasias, basophilic erythrocytic degenerations, differential counts, etc. Briefly stated, no blood diseases were found and no evidence of severe anemias. There was an apparent slight leukocytosis present in 5 cases, many showed a tendency to mononucleosis, while Grawitz's

² Emery R. Hayhurst, Blood-smears, their Preparation and Staining, Jour. Amer. Med. Assoc., December 4, 1909, liii, 1909 to 1911.

(b) No cases of marked pallor being encountered, the hemoglobin was estimated in each case by using simply a Tallqvist scale, the results showing:

[illegible]

4. *Strength of Hand Grip.* This was determined by a hand dynamometer of the Collin type having a graduated reading from 0 to 200 upon the "eschele de traction." The instrument was standardized by obtaining the records of 55 men pursuing all manners of trades and avocations except those of lead exposure; the low reading was invariably over 150 in the weaker hand, the majority of normal men showing a strength of 160 to 230. To get uniformity of conditions, each person was required to stand erect with both arms horizontally outstretched while the hand holding the dynamometer was rather slowly contracted to maximal power, then released. Enough tests were made in each case to be certain maximal power was attained, then the highest reading accepted, gripping alternately with each hand.

These cases with weak grips showed significant associated conditions and findings as follows:

1. Age: 16 of 20 cases over fifty years of age.
2. Time at trade: 16 of 21 cases over thirty years at trade.
3. History of paralysis: 2 of 2 cases.
4. History of plumbism: 10 of 10 cases.

³ L. v. Liebermann and F. v. Fillinger, Ueber Resistenz der Erythrocyten bei gesunden und kranken Menschen, nebst einer einfachen Methode zu ihrer Bestimmung, Deutsch. med. Woch., 1912, xxxviii, No. 10, s. 5.

⁴ Ueber gewerbliche Vergiftungen mit Bezug auf die Liebermannsche Blutprobe, Deut. med. Woch., October 31, 1912, xxxviii, No. 44, s. 3. Note also E. Schaeffer, Fehlerquellen bei Bestimmung der Resistenz der Erythrozyten nach v. Liebermann und v. Fillinger, Deutsch. med. Woch., October 3, 1912, xxxviii, No. 40, s. 2.

5. History of appendicitis: 2 of 2 cases.
6. Unhealthy appearance: 8 of 10 cases.
7. Emaciation of arms: 5 of 5 cases.
8. Inguinal hernia (past or present): 7 of 9 cases.
9. Absent abdominal reflex: 11 of 12 cases.
10. Absent knee-jerks: 3 of 3 cases.
11. Low systolic pressure: 3 of 3 cases.
12. Drop in systolic pressure after exercise: 4 of 4 cases.
13. Too great a relative proportion of the following cases was also associated with weak grips: Interior painters, Germans, Hebrews, history of encephalopathy, father a painter, alcoholics, loss of strength, loss of weight, anorexia, bad taste, salivary disturbance, distension of abdomen, headaches, vertigo, syncope, insomnia, confusion, poor memory, muscular cramps, trembling, incontinence of urine, nocturnal frequency of urination, premature age, lead deposit in gums, arteriosclerosis, incoördination, absent wrist reflexes, dermatographia, lead in urine, atypical blood-smear pictures, decreased percentage of hemoglobin, increased red-blood cells, resistance to hypotonic salt solutions, weakness in wrist extension, and high pulse pressure.

5. *Strength of Wrist Extension.* This was determined also by the dynamometer. The subject was requested to sit in an arm-chair, first with hand passively flexed over forward end of the arm of the chair, when, with a wet towel folded up and placed on the dorsum of the hand to keep instrument from causing pressure pain to the hand, and also to prevent its slipping, the subject was asked to raise his hand up against the examiner's resistance on the dynamometer (active resistance). This gave one reading, the minimal for which was ascertained as not less than 30 with normal men. Secondly, the subject was requested to support his forearm on the arm of the chair, with hand extended free in the air, the wet towel applied as before, after which the examiner, with instrument in hand, forced the subject's hand to flex downward against his passive resistance. This gave a second reading, the minimal for which was ascertained as not less than 35 with normal men.

The results with painters showed:

Active resistance below normal in	16 of 96 cases in both wrists
"	"	"	.	.	20 of 96 " right "
"	"	"	.	.	22 of 95 " left "
Passive	"	"	.	.	7 of 81 " both "
"	"	"	.	.	13 of 81 " right "
"	"	"	.	.	20 of 81 " left "

It is worthy of note that these painters were relatively stronger in the left hand and forearm, the one least used, than in the right; also that weakness in grip (prehension) was much more frequent and pronounced than weakness in wrist extension. These facts

6. *Blood-pressure.* This was determined with a mercury manometer (Mercer type) applied to the right arm, with the subject in a sitting posture, using the stethoscope applied to the cubital fossa to interpret the results. By this means the systolic pressure was first taken, then the diastolic, after which the patient was requested to perform a uniform exercise; namely, that of bending forward, if possible to touch the toes, and rising erect ten times. Thereafter he seated himself at once in the chair at the instrument and pressures were again determined.

[illegible]

⁶ Sphygmomanometry and Pachon's Oscillometer, British Med. Jour., January 13, 1912, No. 2663, p. 72.

Thirty-five cases in which systolic blood-pressure was 132 mm. or over showed significant association as follows:

1. Age, 10 of 20 cases over fifty years old.
2. Time at trade, 12 of 22 cases over thirty years at trade.
3. History of encephalopathy, 4 of 5 probable cases.
4. Alcoholics to excess, 21 of 27 cases.
5. Arteriosclerosis (radial), 8 of 11 cases.
6. Wrist reflex absent, 2 of 2 cases.
7. Abdominal reflex absent, 10 of 12 cases.
8. Knee-jerks absent, 3 of 3 cases.
9. "Gouty" great toe-joint, 6 of 8 cases.
10. Albumin and casts, 5 of 7 cases.
11. There was also associated too great a relative proportion of the following complaints and afflictions: History of plumbism, history of "triad," history of rheumatism, history of coffee excess, loss of weight, vomiting, constipation, diarrhea, visceralgia, distention of abdomen, headaches, depression, poor memory, joint pains, muscular cramps, "rheumatism," tinnitus aurium, urinary and circulatory disturbances, premature old age, pyorrhea, tremor, incoördinations, heart disease or enlargement, hernia, absent cremaster reflex, lead in urine, atypical blood-smear pictures, increase of red-blood cells resistance to hypotonic salt solutions, decreased percentage of hemoglobin and weak hand grips.

Diastolic Pressure. This varied from 62 to 112 mm. with 15 cases over 90 mm.; 14 of these higher diastolic pressures occurred in cases with abnormally high systolic pressures.

Pulse Pressures. This varied between 30 and 97 mm. There were 79 between 35 and 60 mm. There were 8 over 60 mm., all occurring with high systolic pressure. There were 13 under 35 mm., all occurring with low systolic pressure.

Systolic Pressure after Exercise. Rose from 1 to 30 mm. in 91 cases; remained the same in 5 cases, and dropped in 4 cases.

Diastolic Pressure after Exercises. Rose a few millimeters in 8 cases; remained the same in 74 cases; dropped a few millimeters in 17 cases. However, there is no apparent relation between these slight variations and the pressures previously noted, nor with any particular group of symptoms.

Of the total of 100 men, 83 were examined in the afternoon, 12 in the forenoon, and 5 in the early evening.

Although blood-pressure determinations of one sitting cannot be given too much reliance, still the fact that in fully one-third of the cases the findings were at or above the upper limit of normality has some significance. This is particularly so when we take into consideration the report of Mr. John A. Runnberg, the statistician of this same union, issued March 1, 1913, from which I quote:

"A recent investigation as to the causes of death of 100 members during the last four years, reveals the fact that the five great

causes of death are organic heart disease, pulmonary tuberculosis, nephritis, pneumonia and accident at work. Almost one-fourth of all deaths are due to some disease of the circulatory system, of which organic heart disease alone exceeds the general death-rate of the city by about 32 per cent. The investigation further shows that the average age at death from any of these five causes is from two to seven years less than the corresponding death-rate in the city at large."

SUMMARY. Of 100 painters examined under favorable conditions: (a) Definite symptoms of acute plumbism could not be said to obtain in any case. There were no acute abdominal or nervous cases, none showing erythrocytic basophilia in significant amount (that is nothing approaching 1 per cent. of the total number of red cells). However, 2 cases, gave a positive Liebermann hemolytic resistance test and 2 others exhibited lead in the urine, and there was a suggestion of traces in others. (b) Symptoms, signs or after-effects of chronic plumbism of varying degrees, after eliminating other factors, so far as possible, were found in a total of 70 cases. It is not easy to summarize these records, but they fall fairly well into the following groups:

Group 1 (history, symptoms, physical signs, tests). Includes 19 men who gave a clear history of previous lead poisoning, 12 of a history suggestive of lead poisoning, 7 were suffering at the time from symptoms clearly indicative of chronic plumbism, and who, in addition, exhibited physical findings and abnormal results in one or more of the tests described above (not including the sodium sulphide test). Average age, 46.16 years, and time at trade 28.15 years. Only 4 were under forty years and 1 over sixty years of age.

Group 2 (history, symptoms, physical signs). Includes 16 men; 7 with a clear history of plumbism and 9 with a suggestive history. All were suffering from symptoms ascribable to chronic plumbism, and were found by physical examination to have systemic diseases ascribable to chronic toxemia. Special tests were negative or borderline only. Average, 34.56 years, and time at trade 16.75 years. Only 3 were over forty years.

Group 3 (history, symptoms, tests). Includes 7 men; 3 with a clear history and 4 with a suggestive history of plumbism, complaining of typical symptoms and responding positively to one or more tests. Physical findings negative or in abeyance. Average age, 40.43 years, and time at trade 25.14 years. Decade distribution uniform.

Group 4 (symptoms, physical signs, tests.) Includes 12 men who had no history of former attacks, but who were at the time suffering from typical symptoms, and who had positive physical findings and responded abnormally to one or more tests. Average age 43 years, and time at trade 23.75 years. Decade distribution uniform.

Group 5 (history, physical signs, tests). Includes 5 men; 2 with a clear and 3 with a suggestive history of lead poisoning; not complaining of ill health, but with physical signs pointing to chronic plumbism and with abnormal response to one or more tests. Only 1 under fifty years (a man aged 40 years). Average age, 51.40 years, and time at trade 32.20 years.

The following 11 cases are less distinctive, but must be looked upon as suspicious:

Group 6 (history, symptoms). Five men whose history was suggestive and who complained of more or less typical symptoms, but physical findings and tests were without material significance.

Group 7 (history, tests). Two men had a history of former attacks and had marked weakness of the wrists but an absence of recent symptoms, also other abnormal physical findings.

Group 8 (lead line). Two men showed lead deposits in the gums as the only acceptable manifestation. Alcoholism probable cause of other features.

Group 9 (pyorrhea, weak wrists.) Two men showed pyorrhea and weak wrists only. There was an absence of suggestive history, symptoms, and other features.

With the above groups of workers, age and time at trade have nearly equal curves. Analysis of the four means of arriving at a diagnosis (history, symptoms, physical signs, and special tests) shows:

(a) In the younger men (under forty years the tests above described are most apt to fail, while history, symptoms, and certain physical signs are usually present (Group 2).

(b) Among middle-aged men (forty to forty-five years) there is a small group (a part of Group 3) which fail to show significant physical signs while the other features are present.

(c) A fairly large class (Group 4) composed of men of all ages gave no significant history.

(d) Among men over middle age, forty-five years and above, there is a large class (Group 1) showing evidence of every sort indicative of chronic plumbism.

Among the 30 remaining cases were many with suggestive findings, but the preponderance of secondary factors caused them to be eliminated. These cases were as follows:

One each of diabetes, syphilis, tabes (?), Graves' disease (?), hyperchlorhydria, migraine (since childhood in a young man whose blood-pressure was 145), and senility; 6 cases of cardiac or circulatory disease; 8 negatives; and 9 indefinites.

CONCLUSION. Seventy of 100 painters showed evidence of chronic plumbism. The most frequent factors of value in diagnosing chronic plumbism in painters are:

(a) Significant past history of certain complaints as noted above.

(b) Frequency of certain recent symptoms as noted above.

(c) Neuromuscular abnormalities—as tremor, slight incoordinations, abnormal reflexes, weakened hand-grip, and weakened wrists.

(d) Circulatory disturbances affecting the blood-pressure, the heart, and the urine.

(e) Conditions of the gums—pyorrhea, rarely lead-line.

I desire to acknowledge the valuable suggestions and assistance received from the Director and various members of the staff of the Sprague Memorial Institute; from Dr. Alice Hamilton, and others. I would also state that the coöperation and assistance of the officials, particularly Mr. J. A. Runnberg, and Mr. G. M. Hanson, statistician and secretary respectively of the painter's union from which the men came, deserve mention, while the fact must not be forgotten that every man who was examined volunteered his time and person to promote the undertaking.

FATAL GASTRO-INTESTINAL HEMORRHAGE.

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SUDDEN gastro-intestinal hemorrhage is fortunately not a common cause of death. Hemorrhage is sometimes the fatal termination of enteric fever and other diseases, but the sudden occurrence of gastric and intestinal hemorrhage with those in the enjoyment of practically good health is one of the most alarming incidents in the work of a surgeon or physician. In presenting the following cases, we have excluded those which were considered due to the commoner causes of hemorrhage, such as ulceration of the stomach or bowel, aneurysms rupturing into the tract, blood disorders, or malignant disease. Neither did we include those fatal cases, in which the clinical signs indicated an unusual etiology, but in which no confirmatory postmortem examination was obtained.

CASE I.—A. L., male, aged thirty-three years, was admitted to Dr. Armstrong's service at the Royal Victoria Hospital October 18, 1912. The patient left Toronto on the night of October 17, 1912, perfectly well. After eating a hearty breakfast in Montreal he was suddenly seized with vomiting, and emitted a basinful of

bright red blood. He had to be carried to bed. A second hemorrhage occurred that evening, and he was taken to the Royal Victoria Hospital. An examination of the blood showed it to be normal. The stomach was inspected, but no source of hemorrhage was found; the viscus was full of blood, also the transverse colon. An examination of the stomach mucosa failed to show any erosion or the slightest ulceration, and even after wiping off the mucosa no oozing could be detected at any point.

A postmortem examination was made six hours after death—it was practically one of those negative autopsies in which no demonstrable cause of death could be found. The body was well nourished, of splendid physique, and 165 cm. in length; rigor mortis was present; dorsal lividity absent. Skin was pale; eyes light brown; pupils equal. The chest was bulging. The abdomen was flat. There was a median incision extending from the costal angle downward in the midline 13.5 cm. in length.

There was no abnormality discovered in the circulatory or respiratory systems, excepting signs of obsolescent phthisis in the apices of the lungs.

Digestive System. The esophagus was pale and the epithelium desquamated in places. No varices were found in the esophagus. The stomach was normal in size and contained a small amount of mucoid material and some bright red blood. A posterior gastro-enterostomy wound was present; its edges were a deep purple. The remainder of the gastric mucosa was bright red and contained fluid blood; a few erosions were present, visible only under careful examination, the result apparently of recent operative manipulations. They were inadequate to cause the fatal hemorrhage. The pyloric ring was well-marked, and there was no indication of a recent or chronic gastric ulceration.

The duodenum was 6 c.c. in circumference; it was uniformly congested, and the follicles were enlarged. The contents were blood-stained. There were no signs of duodenal ulcer. The remaining portion of the small intestine showed no ulceration; the contents were composed of brownish clotted blood.

There was no abnormality found in the large bowel, excepting that the contents were intermingled and the bowel distended with tarry blood.

The liver weighed 1020 grams, and measured $20 \times 15 \times 7$ c.c. The organ was small, the edges were sharp, and the cut surface was pale. There were several areas in which the connective tissue of the organ appeared increased, but there was no generalized increase. There was one small fibrous nodule in the substance of the liver, about the size of a small marble, which faded into the surrounding tissue.

Microscopically.—The liver showed a few areas of cirrhosis. The portal connective tissue was slightly increased in amount; necrosis

of the liver cells had occurred in a few situations. Focal collections of inflammatory cells were present in the portal connective tissue. The liver cells for the most part stained deeply, but their contour was obscured.

Gall-bladder. The gall-bladder was full of viscid, yellowish-brown bile, the walls were not thickened; there were no hemorrhages.

Pancreas The pancreas measured $16 \times 3 \times 1.5$ c.c. It showed no abnormality.

Spleen. The spleen disclosed no abnormality. It was not increased in size.

Kidneys. The kidneys showed no fibrosis, and no inflammatory cell infiltration when sectioned. No abnormality was observed in the gross specimen.

Adrenals. The adrenals were cavitated.

A feature of interest was the abundance of hemolymph nodes throughout the upper abdomen and along the aorta.

Blood. The blood showed a greatly delayed coagulation time, and an intense polymorphonuclear leukocytosis was found of the adult and multifid type. Juvenile forms were not noted. The red cells showed no particular change. Some films were full of strepto-diplococci. The two psoas muscles were remarkably friable.

The postmortem examination was unable to throw any light upon the causation of the fatal hemorrhage in this case. The only departures from the normal were: in the liver, which showed some slight areas of fibrosis, and some slight mucosal erosions in the stomach.

The possibilities which exist as to the causations were: (1) That the hemorrhage was the result of diffuse oozing from all parts of the gastric mucosa. (2) That it was a case of hemophilia; there is no evidence in the history of the existence of such a condition.

CASE II.—A. L., male, aged fifty years, was admitted to Dr. Martin's service at the Royal Victoria Hospital for dropsy which began one month before admission. One week before he came to the hospital he had had severe abdominal cramps, jaundice, and clay-colored stools. He had been a heavy drinker. He had marked ascites, and over 1400 ounces of straw-colored fluid were withdrawn from his abdomen at different times during his three weeks in the ward. The night following the last withdrawal he vomited some black material, and the next day about ten ounces of clotted blood. The following day he died in syncope.

The autopsy performed by Dr. Gruner disclosed an interesting condition. The stomach was 32×25 c.c., and was distended with 680 grams of semisolid blood; no gross source of hemorrhage could be found in the stomach or duodenum, but a few mucosal erosions were present near the cardiac end of the viscus, and the lower third of the esophagus contained a number of dilated and prominent veins, evidently the source of the hemorrhage. Some

tarry blood was found in the small and large bowel. In addition to these findings the liver was markedly cirrhotic. The portal vessels were small, and there was marked proliferation of the bile ducts. There was no bile infiltration observable. A condition of perihepatitis was present. Other findings were an hypertrophied spleen; tubercles over the peritoneum; ascites; chronic interstitial pancreatitis; chronic mixed nephritis; arteriosclerosis.

CASE III.—Boy, aged four and a half years, a patient of Dr. J. J. Gillis, of Merritt, B.C., a former house surgeon at the Royal Victoria Hospital, to whom we are indebted for the clinical notes.

When two and a half years old the boy was treated for an illness resembling typhoid fever and liver trouble in a hospital in Vancouver, B.C. The history is not very definite, but he was ill for six weeks. Save for this illness he has always been a healthy child. On the evening before his sickness he ate a hearty supper, and when getting out of bed the following morning he vomited a large quantity of bright red blood. He was hurried to the hospital, and on the way had several hemorrhages; during the day he had two dark-colored bowel movements. For two days he did very well, but on the third day he had two more hemorrhages, and died. Only a partial autopsy was permitted. When the stomach and duodenum were opened blood was found, but no ulcer nor any enlarged varices. A number of pin-pointed hemorrhagic spots were noticed over the stomach. The stomach and duodenum were sent to one of us for examination, but there was nothing found to account for the source of the hemorrhage.

CASE IV.—M. B., female, aged seventy years, service of Dr. Martin; found in moribund state; no history obtainable; superficial abdominal veins were prominent; marked edema of legs and abdominal wall; ascites; died few hours after admission to Royal Victoria Hospital. Postmortem by Dr. Grunner: Cirrhosis of liver; hemorrhage into the stomach, duodenum, and jejunum; unruptured aortic aneurysm; general arteriosclerosis.

CASE V.—D. McK., male, aged thirty-eight years; service of Dr. Hamilton; marked alcoholic history; brought to outdoor department and was unable to give a coherent account of his illness. Jaundiced; died a few hours after entrance. Postmortem by Dr. Gruner: Fatty liver; enlarged esophageal veins; hemorrhages into the stomach; mitral stenosis; fatty heart; ascites; fibrosis of the spleen.

COMMENTS. The etiology of cases of sudden gastric hemorrhage similar to those we have outlined is not clear in every instance. W. J. Mayo is of the opinion that "where gastric hemorrhage accompanies cirrhosis of the liver, splenic anemia, and disordered blood states it may be attributed to toxic erosions of the gastric mucosa." Although the nature of the toxic process is not well understood, yet evidence is not wanting which indicates that in

a certain number of these cases microorganisms are the causative agent.

The majority of observers are inclined to the view that the gastro-intestinal hemorrhages occurring in the newborn are of toxic origin; thus Litzenberg reported the finding of Friedländer's bacillus from hemorrhagic areas, found in a case of fatal hemorrhage in a child, two days old.

Cases of purpura are of common occurrence; the type associated with Henoch's name is usually characterized by submucous gastro-intestinal hemorrhages, severe abdominal pain, tenderness, and distention; purpura and effusion into the joints are also present. In his original paper on the subject in 1874 he reported four cases, all under fifteen years of age, in which recovery took place after repeated attacks.

Howard, in 1899, expressed the view that organisms of the *Bacillus mucosus capsulatus* group as well as streptococci were able to induce hemorrhagic septicemia, accompanied by gastro-intestinal hemorrhages, by a degenerating action on the bloodvessels leading to rupture, as well as destruction of the red blood cells themselves.

As is well known, there are many varieties of bacilli loosely classified under the term *Bacillus mucosus capsulatus*; while their ability to induce hemorrhage may not characterize all, yet it seems to be a quality of some of this group. Howard was able to isolate a variety of the *Bacillus mucosus capsulatus* in a fatal case of hemorrhagic septicemia which showed cultural peculiarities at variance, with other well-known members of this group.

Hemorrhagic peritonitis has been produced in rabbits, by inoculations with the fluid, from fatal causes of hemorrhagic peritonitis, and different observers have recovered apparently different organisms from such cases.

Jacobson and Post, in drawing attention to hemorrhage from the stomach or intestines, occurring as an initial symptom without pathological disorganization of the mucosa of any kind, recorded several interesting cases. They expressed the view that "certain microorganisms, particularly those possessing the characteristics of the pneumococcus are capable of provoking severe hemorrhage in various parts of the body and that gastric and intestinal hemorrhage can be the first evidence of such a toxemia."

Bolton is of the opinion that a form of erosion of the gastric mucosa which he calls acute gastric ulcer is to be found in many of those obscure cases of severe and fatal hematemesis.

The erosion is often difficult to detect, requiring special mounting in postmortem specimens. It may not be strictly correct to designate these minute erosions by the name of ulcer, and, furthermore, many are inclined to the view that they are of toxic origin.

An interesting collection of cases of fatal gastro-intestinal

hemorrhage was recorded by Preble in 1900; 56 from the literature and 4 which came under his observation. All were found at autopsy to have cirrhosis of the liver. Of these 60 cases the source of the hemorrhage was found in 20 to be from ruptured varices at the lower end of the esophagus. In 15 others the varices were shown, but there was no evidence to the effect that the hemorrhage originated there. In 6 cases the gastro-intestinal mucosa was normal throughout, and no varices were present. The records were not very complete in the remaining cases. In 5 death occurred from the first hemorrhage. Another feature of interest in Preble's collection was the early age of many of the patients. Thus the case reported by Taylor was only five years old. Had had jaundice four months before; liver and spleen were enlarged; later, had ascites and edema; paracentesis. A few days later death after hematemesis. Stomach was full of blood; no erosion or ulceration; liver small; spleen enlarged. The average age of the cases in Preble's collection was close to thirty-five years. Some of his conclusions were that fatal gastro-intestinal hemorrhage is an infrequent but not rare complication of cirrhosis of the liver; that in one-third of the cases the first hemorrhage is fatal, in the other two-thirds the hemorrhages continue at intervals over a period varying from a few months to eleven years; that esophageal varices are present in 80 per cent. of the cases, one-half of which show, macroscopic ruptures; that the cases in which no varices are present are probably due to simultaneous rupture of many capillaries of the gastro-intestinal mucosa; that in only 6 per cent. of the cases which show esophageal varices is the cirrhosis typical, that is, show ascites, enlarged spleen, and subcutaneous abdominal varices.

We are inclined to support the view that the erosions found in the stomach, in some of the fatal cases of hematemesis, are of toxic origin, the nature of which is not definitely known. And it is not improbable that the cirrhosis of the liver found so frequently in these cases is an effect of toxic processes. While there is no definite proof to support the view, yet it is not inconceivable that the infection may have been present in the gastro-intestinal tract for some time, producing effects not severe enough to attract attention. The history of an illness resembling in some features an enteric infection, as well as the varying ages at which the condition may be found, lends some color to this supposition.

The ruptured varices found at the lower end of the esophagus, in cases in which cirrhosis of the liver was also present, explain the source of the hemorrhage in one group of these cases.

The veins of the cardiac end of the stomach are part of the portal circulation, while the esophageal veins are not, there are in this situation connecting links between the two systems, their close proximity to the seat of obstruction aids the formation of

varices; and it is probable that any sudden interference with the circulation might rupture their thin walls. It is possible that interference with pressure, following paracentesis may have been the explanation of the fatal hemorrhage in one of our cases. While this explanation accounts for the hemorrhage in a certain number of cases, yet for the group in which no varices are found, and in which little or no liver cirrhosis is present, another cause must be sought.

An increasing number of cases are being reported in which gastro-intestinal hemorrhage is the most striking feature, and which show at autopsy negative findings; another feature in the majority of these cases is the sudden onset of the hemorrhage.

This group of cases of fatal hematemesis may be attributed to the direct or indirect effect of microorganisms, and it is likely that more attention will be directed to them when our knowledge of the bacteriology of the gastro-intestinal tract is further advanced than at present.

C. A. Ewald thinks that in the female, vicarious menstruation accounts for some cases of severe gastro-intestinal hemorrhage, while other cases may occur from the rupture of diseased arteries in the crisis of tabes. He reports two fatal cases, one in a male, age twenty-four years, the other in a male, aged forty-eight years, in which the autopsy failed to disclose the cause of the hemorrhage.

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THE PROCESS OF BONE REPAIR FOLLOWING TRAUMA.

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THE process of the repair of bone after trauma seems to be more or less shrouded in mystery. In reviewing the literature one finds the greatest diversity of opinion. This is largely to be attributed to two facts: (1) that clinicians have reported results frequently

without consulting the microscopic findings, and (2) that satisfactory microscopic examinations are difficult because of the injury incurred by the soft parts while the bone is undergoing decalcification. Some authors invest the periosteum with bone-reproducing qualities, while others claim that it is nothing but a limiting membrane.

In the embryo there are two types of primary ossification, intramembranous and intracartilaginous.

INTRAMEMBRANOUS OSSIFICATION. The basis for development is embryonal connective tissue or mesenchyme. At certain points these embryonal connective-tissue bundles become impregnated with calcium salts, the cells in each of these areas increase in number, some of them becoming more or less round or oval, with distinct nuclei and a considerable amount of cytoplasm, and arrange themselves in single, fairly regular rows along the bundles of calcified fibers. These differentiated cells are known as osteogenetic cells or osteoblasts. Under the influence of the osteoblasts a thin layer of calcium salts is deposited between the osteoblasts and the calcified fibers forming true bone. Successive layers of calcium salts are laid down, enclosing some of the osteoblasts, which then become bone cells. The spaces in which the bone cells lie are called lacunæ.

INTRACARTILAGINOUS OSSIFICATION. In this type of ossification the bone is preformed from hyaline cartilage, which is also derived from embryonal connective tissue. Around this cartilage is a fibrous connective-tissue membrane called the perichondrium. This membrane gradually fades on the one side into cartilage and on the other into the surrounding connective tissue. There is no sharp dividing line. During the early stage, calcium salts are deposited in the matrix of the cartilage, forming an "ossification centre." Later small bloodvessels push their way in from the perichondrium of the new diaphysis, carrying with them some of the embryonal connective tissue. These ingrowths of bloodvessels and connective tissue are called periosteal buds. The septa between the cartilage cells break down, forming large spaces into which the periosteal buds grow. Many of the connective-tissue cells are transformed into osteoblasts, and with the fibers and bloodvessels constitute osteogenetic tissue. This process continues until the primary spongy bone is formed, this being later destroyed by osteoclasts, with a subsequent formation of compact bone.

It is evident from this brief *resume*, that bone in the embryo is formed by a metaplasia from the connective tissue, accompanied by a deposition of calcium salts. Of interest in this connection is the work of Gideon Wells, who has shown that if cartilage is transplanted into the omentum it has a greater power of absorbing calcium from the blood than any other tissue similarly placed.

THEORIES IN REGARD TO BONE REPAIR. 1. *Periosteum the Main Agent in Repair.* This has been recently the most generally

accepted theory. The adherents of this theory consider that the periosteum is a specialized tissue for the formation of new bone, and that bone deprived of its periosteum will eventually die. Much experimental work has been done along these lines. Numerous investigators have transplanted periosteum and observed new growth of bone. MacEwen has offered the criticism that in removing the periosteum a layer of bone cells, osteoblasts, are transplanted also. If a piece of the periosteum, to be transplanted, were saved for microscopic examination this question could be satisfactorily solved. Morpugo demonstrated that the periosteum of a corpse would reproduce new bone when implanted after one hundred and sixty-eight hours. Murphy thinks that if periosteum be transplanted in the same individual, especially if he be young, it will form a lasting bone deposit; but if transplanted into another individual, it rarely produces bone. He, however, states that bone transplanted with or without its periosteum into fat or muscle tissue eventually dies. MacWilliams, in a paper read before the American Medical Association, states that periosteum is necessary for the life of bone transplants, unless the transplants are very small, in which case they grow and unite without periosteal aid. He has demonstrated in his experimental work that large bone fragments transplanted into the soft parts will live if the periosteum be attached, but that they are almost constantly absorbed when transplanted without the periosteum.

2. *Periosteum not a Bone-forming Organ.* MacEwen considers the periosteum to be merely a limiting membrane without osteogenetic functions. He has performed numerous experiments which seem very convincing, although it is frequently difficult to understand his deductions. He has, for instance, removed about 1 cm. of the radius, scraped off the periosteum, and cut the piece removed into small fragments, which were reinserted between the cut ends of the radius. Eleven weeks later the animal was killed and the leg examined. To quote from MacEwen: "Small diaphyseal grafts, when placed in a gap in the continuity of bone, show active proliferation from the whole circumference, each piece being an ossifying centre from which osseous tissue is thrown out sufficient to fill the gap between the various fragments and to unite them together along the two ends of the divided bone."

MacEwen and MacWilliams have both shown that small fragments of bone transplanted into the soft parts will unite and form definite bone, although MacEwen has not allowed time enough to see if the bone would eventually be absorbed.

In transplanting sections of the diaphysis, most authors are united in thinking that the transplanted piece dies, but that union occurs by new bone growing in from the shaft of the host, and also by new bone forming in the Haversian canals and medulla of the transplanted piece.

Barth can see degeneration in the nuclei of the transplanted fragment in one week; in young animals he sees small groups of bone cells until the twenty-second day.

Axhausen has transplanted joints and bones into soft parts, and finds three stages in the transplanted piece. (1) the nuclei take a normal stain; (2) the nuclei become crumpled and distorted; (3) the nuclei disappear and the bone becomes homogenous.

On the other hand, Takata finds that isolated bone fragments are surrounded by irregularly lying, dentated, relatively large cells that closely resemble osteoblasts. These cells are not separated from the surrounding connective tissue, and they lie without any sharp differentiation. The connective-tissue cells become gradually larger as they approach the bone. He considers these fragments to be living bone.

Of great interest is the formation of bone in arteries, new-growths, etc. Bunting, Harvey, Wells, and others have described the formation of true bone in arteries. In Bunting's case there was a formation of bone in a sclerotic aorta. This tissue had a definite lamellar structure with Haversian canals, and a narrow cavity, containing the normal cellular elements. He made a careful histological study, and his conclusions were as follows: "Bone in arteries may be deposited in two ways; either by the conversion of connective tissue into a callous or osteoid tissue, with subsequent conversion into bone and at times with the formation of cartilage, or by the resorption of calcified tissue by vessels and osteoblastic membrane, derived by metaplasia from the connective-tissue cells accompanying the vessel."

Wells believes the reason bone is so rarely deposited in veins is that the excess of carbon dioxide in the venous blood keeps the calcium in solution.

Harvey gives the following theories for the formation of bone in arteries: (1) wandering osteoblasts; (2) metaplasia of connective tissue; (3) metaplasia of mesothelium of blood capillaries. He produced new bone in the aorta of rabbits by painting the adventitia with 3 per cent. solution of silver nitrate, or 2 per cent. solution of copper sulphate. He killed them after various lengths of time, varying from one hundred and ten to one hundred and eighty-six days, and found calcium plaques along the inner edge of the media. On sectioning these plaques he found definite lamellar bone, with Haversian canals, lacunæ, and red marrow cells.

Liek, Posehariseky, Sacerdoti, and Frattin have tied off in rabbits the renal vessels on one side. In from sixteen days to two months the animals were killed. True bone was found adjacent to the calcium deposits in the necrotic connective tissue of the kidney; this was accompanied by a growth of granulation tissue inward from the capsule. Here also was definite lamellar bone.

The writer's work was undertaken to attempt to learn the method

of repair in bone cavities. To accomplish this, Dr. Clarke, director of the surgical research laboratory of Columbia University, suggested making simple cavities in the diaphysis of the humerus in dogs. An effort was made to secure a cavity in which absolute hemostasis occurred, and therefore a dead space. The humerus was exposed, usually by a median incision, the periosteum was removed for a distance of at least 3 cm. in length and for almost the entire circumference of the bone. A rectangular piece, 1 x 0.6 cm., extending into the medullary canal, was removed from the median surface of the diaphysis, and the medullary cavity was thoroughly curetted and packed until hemostasis occurred. Realizing that this hemostasis was only temporary, and that oozing probably occurred from the medullary cavity after suturing the muscles over it, various experiments were tried: (1) the cavity was packed and then filled with hot sterile oil and the wound closed; (2) the cavity was packed with gauze, which was removed in twenty-four hours; (3) the cavity was packed with gauze sterilized in oil, which was removed twenty-four hours later (the purpose of this was to prevent the gauze adhering to the sides of the bone cavity and the subsequent oozing upon its removal); (4) both ends of the cavity were filled with Morehof's bone wax; this caused very good hemostasis, and was used in the largest number of experiments.

In one case a sac was made of the peritoneum covering the appendix. The peritoneum was stripped off and a purse-string suture applied around the opening of the peritoneum; the sac was then filled with salt solution and placed in the bone cavity, completely filling it. The idea was to prevent the cavity from filling with blood clot, and with the hope that the sac would be eventually absorbed. Unfortunately this dog received a gas bacillus infection and died in forty-eight hours.

After varying lengths of time the dogs were killed and the legs hardened in formalin. The gross appearance was then noted. Longitudinal or cross-sections were made. After decalcifying they were sectioned and examined microscopically. It has been a difficult thing to sufficiently decalcify the bone without destroying the soft tissue.

RESULTS. Thirty-eight dogs have been operated upon as described above. Of this number, 4 died of acute infection, 4 sustained fractures following operation, and 6 died of either distemper or lobar pneumonia before a satisfactory length of time had elapsed. The remaining dogs were killed at varying lengths of time, ranging from thirty to one hundred and ninety days. A certain definite type of repair occurred in most of these cases. On cutting down upon the humerus a cavity containing a serosanguinous fluid was entered. The base of this cavity was bare bone of the diaphysis, while the periphery consisted of a flat connective-tissue layer that was continuous with the overlying muscles. These cavities varied from 2

to 5 cm. in length, and in some cases extended around almost the entire circumference of the bone. In the bare bone at the base of this sac was found the former bone cavity extending into the medullary canal. Extending upward from the bottom of the cavity was a pyramidal mass of tissue which microscopically resemble granulation tissue. On microscopic examination this tissue was found to contain a ground-work of granulation tissue, with deposits of calcium salts arranged around the perivascular areas.

In a few cases a definite connective-tissue layer, continuous with the periosteum and adherent to the surrounding structure, has grown over the bone and the cavity has been repaired under this.

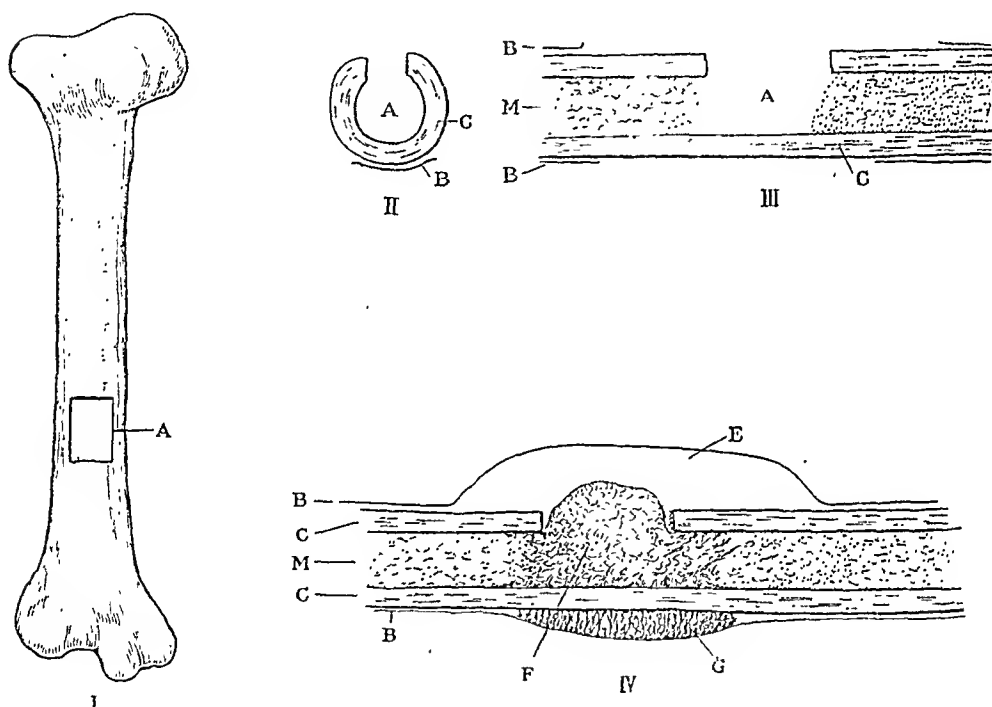


FIG. 1.—Schematic drawings. *I*, cavity in shaft; *II*, transverse section through bone and cavity; *III*, longitudinal section; *IV*, manner of repair of bone cavity. *A*, cavity; *B*, periosteum; *C*, shaft; *E*, cavity under periosteum filled with serosanguinous fluid; *F*, new-forming bone; *G*, bone forming under periosteum; *M*, medullary cavity.

The four cases of fracture were sectioned and studied. Here there was seen a gradual transition of connective tissue into bone. It was impossible to make out any definite periosteum.

In giving detailed accounts of experiments only those are given where it has been possible to get good photomicrographs. Those not mentioned have all been examined microscopically, and all show a similar process of repair to those given in detail. It seemed wise to omit giving their histories in detail on account of taking up too much space.

Dog No. 362. Surgical Research Series, 1912-1913. Experiment No. 21. Surgical Pathology, No. 2066. Operation, May 27. Death, due to pneumonia, June 8. Duration, twelve days. Median incision, 6 cm. long, over left upper foreleg. Humerus exposed. Periosteum removed for a distance of 3.5 cm. A rectangular piece of bone, 0.8 x 1 cm., was removed from the shaft. This incision extended into the medullary canal, which was everted and packed for several minutes. Upon removal of the packing, good hemostasis was observed. The muscles were sutured over the defect in the shaft, and the skin was closed with continuous silk.



FIG 2.—Surgical pathology; No. 2066. Longitudinal section through one-half of cavity. Duration, twelve days. A, edge of bone cavity; B, new forming bone; C, blood clot.

Autopsy. Lobar pneumonia of right upper lobes. Incision wound on leg perfectly healed. Leg hardened in formalin. Upon cutting down on the humerus a small sac, about 2 cm. long by 1.5 cm. wide, is opened. The base of this sac is the humerus and the apex consists of a smooth fibrous tissue membrane apparently continuous with the overlying muscles. This sac contains a sero-

sanguinous fluid. In the humerus at the base of this sac is the aperture in the shaft, which is filled with blood clot.

Microscopic Examination (Figs. 1 to 3). A longitudinal section was made through the humerus. The bone was decalcified with phloroglucin and nitric acid solution. Plate I shows a schematic drawing of the operation and longitudinal sections taken for microscopic examination. The periosteum does not approach the aperture in the shaft for at least a distance of 1 cm. in all directions. Growing up from the base of the medullary canal and from its upper limits is seen a granulation tissue staining a deep blue. This tissue is made up of fibroblasts and other connective-tissue cells. One

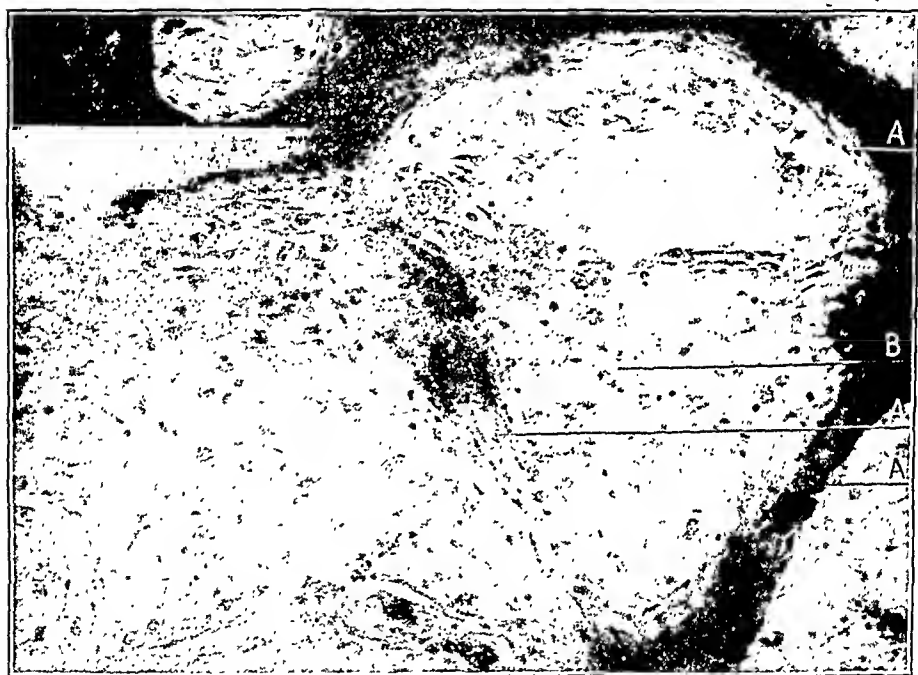


FIG. 3.—High power of part of Fig. 2. A new-forming bone, stellate-shaped cells; B, arcular connective tissue.

sees a net-work of tissue taking a purple stain which, under high power, is seen to be bone. One is impressed with the idea that calcium salts have been laid down upon ordinary granulation tissue in the perivascular areas; that is, in the areas farthest from the bloodvessels. This is an early formation of new bone.

Dog No. 127. Surgical Research Series, 1912-1913. Experiment No. 29. Surgical Pathology, No. 2237. Operation, December 3, 1912. Died December 19, of pneumonia. Duration, fifteen days. Operative procedure similar to Pathology No. 2066. Healing of operative wound *per primam*. Longitudinal sections made in routine manner. Upon gross inspection the periosteum found

separated from the bone about 0.5 em. on all sides of aperture in humerus. This bone cavity is seen filled with blood clot.

Microscopic Examination (Fig. 4). The centre of the cavity is seen to be filled with blood clot, and fine interlacing strands of new bone are being formed from the connective tissue. Under high power of the new bone one sees numerous round cells, with dark staining eccentric nuclei. It is possible that these cells are either converting the earlier bone into a denser bone, or they may be phagocytes.

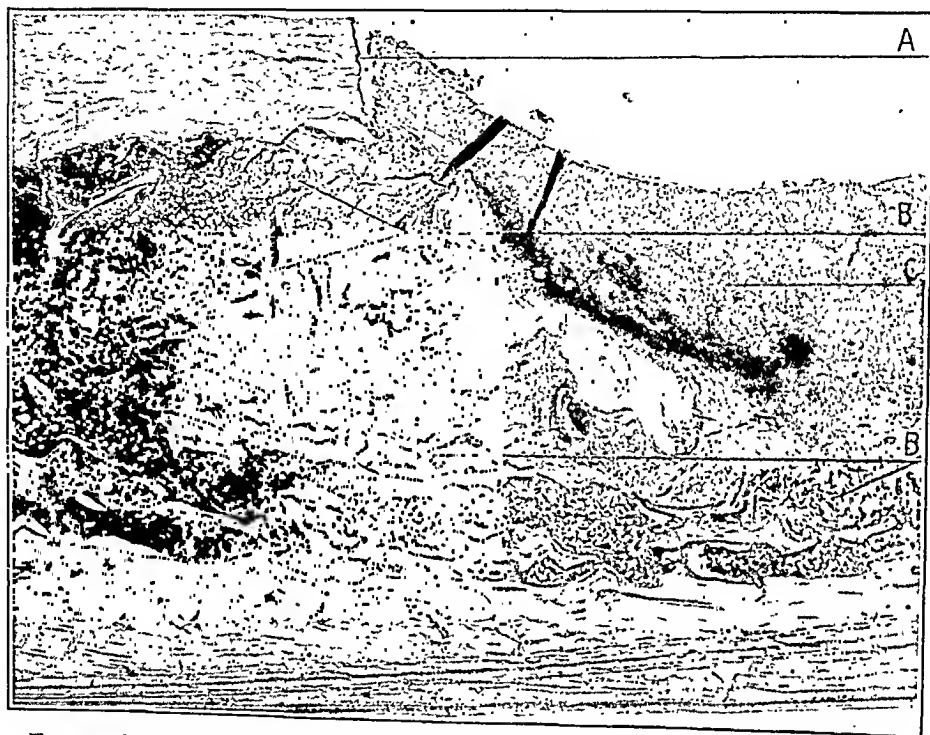


FIG. 4.—Surgical pathology, No. 2237. One-half bone cavity. Duration, fifteen days.
A, edge of bone cavity; B, new bone; C, blood clot.

Dog No. 108. Surgical Research Series, 1911–1912. Experiment No. 4. Surgical Pathology, No. 1882. Operation, January 5, 1912. Died of pneumonia February 14, 1912. Duration, twenty-four days. Routine operation.

Autopsy. Lobar pneumonia. Operative wound healed *per primam*. Upon cutting down upon the humerus a sac containing a serosanguinous fluid was opened. This fluid, upon microscopic examination, contains numerous erythrocytes, polymorphonuclear leukocytes, and lymphocytes. The base of this sac is bare bone; in the centre is the aperture in the humerus. The apex of the sac is a smooth, connective-tissue membrane continuous with the overlying muscles. The periosteum is well separated from the bone cavity. The centre of this aperture is filled with a growth of new tissue resembling granulation tissue in appearance; on palpating

this with a needle it is hard and gritty. On longitudinal section this tissue filling the bone cavity is seen to be an early formation of new bone.

Microscopic Examination (Figs. 5 and 6). This bone-granulation tissue arises from the base of the cavity; it has a honey-combed appearance, the lighter staining areas consisting of bloodvessels and connective-tissue stroma, while the darker stained areas are

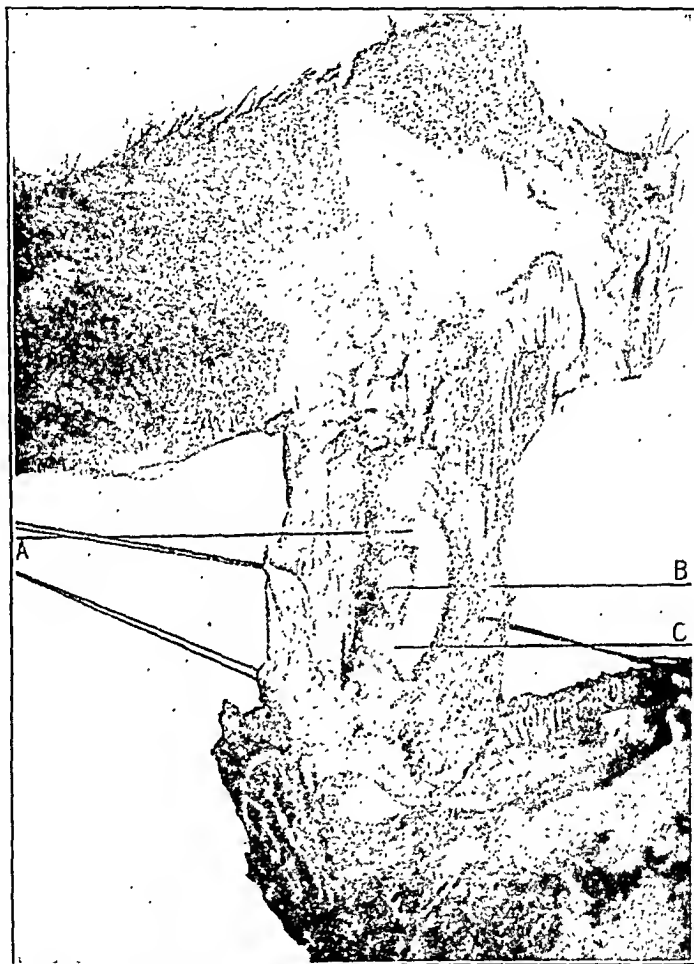


FIG. 5.—Surgical pathology, No. 1882. A, edge of periosteum; B, new bone filling cavity; C, bare bone.

newly forming bone. Here under high power one cannot see that any specific cell forms this bone; it appears rather that calcium salts have been deposited in the perivascular areas upon connective tissue.

Dog No. 361. Surgical Research Series, 1911-1912. Experiment No. 20. Surgical Pathology, No. 2147. Operation, May 27, 1912. Killed October 15, 1912. Duration, 141 days. Piece,

1 x 0.5 cm., removed from lateral surface of left humerus; cavity curetted thoroughly; medullary canal at both ends filled with bone wax. Excellent hemostasis. Muscles and skin sutured in usual manner.

Autopsy. Only slight linear operative scar visible; on palpation the bone feels smooth; no depression or nodules can be felt. On cutting down upon the bone a cavity, 5.5 cm. long by 1.5 cm. wide, is opened; it extends from immediately above the condyle



FIG. 6.—Low power. Longitudinal section of Fig. 5. A, edge of bone cavity, living bone; B, new bone; C, connective tissue; D, bloodvessels and areolar tissue.

to 1 cm. below the greater trochanter. This cavity contains a small amount of serosanguinous fluid; its base is formed by bare bone. The centre surface is a fibrous tissue membrane adherent to and apparently continuous with the adjacent muscles. On the humerus about 0.5 cm. below the upper limit of this sac is a small oval depression in the bone; it measures about 4 mm. in diameter and 2 mm. in depth. At the bottom of this depression is a small shot-like piece of bone which has the appearance of a sequestrum; x-rays,

however, show there is no sequestrum, but there is a definite rarefaction of the bone at this location.

Microscopic Examination (Figs. 7 and 8). The bone which bridges over the aperture is much more cancellous than normal; the Haversian canals occur more frequently, and are larger. The bone cells are present and stain with hemotoxylin and cosin. In the small piece at the bottom of the depression the cells appear

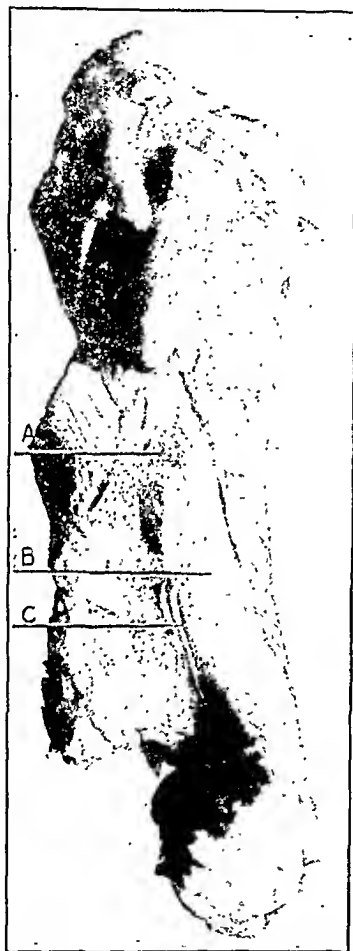


FIG. 7 —Surgical pathology, No. 2147. Duration, one hundred and forty-one days. A, bone cavity; B, bare bone; C, periosteum.

shrunk and stain poorly, but it has not the appearance of dead bone, as the cells and Haversian canal systems can be clearly made out. Immediately below this bridge, in the medullary canal, is a cavity, which before decalcification was filled with bone wax and blood-clot; around this is a thin capsule of new bone. In this case the bone has reformed, with the periosteum stripped off from the bone for a distance of 5 cm. This bone is living bone; the process of repair is probably a later stage to the previous cases.

Dog No. 392. Surgical Research Series, 1911-1912. Experiment No. 24. Surgical Pathology, No. 2148. Operation, June 17, 1912. Killed October 15, 1912. Duration, one hundred and twenty days. A piece, 1×0.8 cm., removed from the median surface of right humerus; the medullary canal was thoroughly curetted and packed; after removing the packing good hemostasis was observed. Muscles and skin sutured in usual manner.

Autopsy. Only a linear scar visible; humerus feels smooth. On cutting down upon the bone a sac similar to Pathology No. 2147 is opened. It is difficult to observe where the aperture was in the humerus; there is a very slight depression in the bone.



FIG. 8.—Low power of Fig. 7. A, new-forming bone; B, new-forming bone, showing enlarged Haversian canals; C, base of cavity A in Fig. 7.

Microscopic Examination (Figs. 9 and 10). The most noticeable thing in the new bone is the direction of the Haversian canals. Instead of running parallel to the surface they lie perpendicular to it, so that it is easy to determine the junction of old and new bone. In the medullary cavity numerous strands of bone are seen running toward the new bone. In comparing this section with Pathological No. 1882 it would seem that this is a later stage of a similar

type of repair; the direction of the Haversian canals indicate that it originated from the tissue of the medullary canal.

- Dog No. 325. Surgical Research Series 1911-1912. Pathological, No. 2180. Operation, May 6, 1912. Died December 7, 1912. Duration, one hundred and ninety days. Cavity made in humerus in usual manner, good hemostasis. Wound healed *per primam*. Animal in good shape; killed by chloroform.



FIG. 9.—Surgical pathology, No. 2148. Duration, one hundred and twenty days. *A*, depression at situation of former bone cavity; *B*, bare bone; *C*, periosteum.

Autopsy. On cutting down upon humerus it is difficult to find the site of the former operation, only a slight depression being visible. The bone is completely covered with fibrous tissue continuous with periosteum and adherent to the overlying muscles.

Microscopic Examination (Fig. 11). The aperture in the shaft is almost entirely filled with new bone. In this portion, however, the Haversian canals run perpendicular to the surface rather than horizontal to it. Spicules of new bone are seen traversing through the tissue of the medullary canal immediately beneath the former aperture.



FIG. 10.—Longitudinal section of Fig. 9, under low power. A, edge of former cavity—Haversian canals run perpendicular to surface; B, bone strands; C, bone at bottom of cavity.

Dog No. 88. Surgical Research Series, 1911–1912. Experiment No. 2. Surgical Pathology, No. 1907. Operation, January 12, 1912. Cavity in humerus by usual method. On January 24, the dog jumped off a chair and fractured the foreleg. Animal killed with chloroform February 21. Duration following fracture is twenty-eight days.

Autopsy. Wound in leg healed; there is non-union, with considerable over-riding of the fragments. There is considerable thickening about the ends of the bone. On cutting down upon the humerus one finds marked callous formation.

Microscopic Examination (Fig. 12). There is new bone proliferating from the outer surface of the ends of the fractured bone; no definite periosteum can be made out. Under high power

one finds a definite metaplasia from connective tissue to fibrocartilage, from connective tissue to bone, and from fibrocartilage to bone. In the areas of new-bone formation one finds first a layer of fibrous connective tissue that gradually changes into newly forming bone. There are all stages of metaplasia between the cartilage and the bone cells. The nuclei becomes irregular, often stellate, the deep blue of the capsule gradually fades and eventually disappears, and the cell takes on all the characteristics of the bone cell.



FIG. 11.—Surgical pathology, No. 2180, under low power. Duration, one hundred and ninety days. *A*, section of former bone cavity—Haversian canals run perpendicular to surface; *B*, junction of old and new bone; *C*, bone spicules in medullary cavity; *D*, bare bone.

Dog No. 251. Surgical Research Series, 1911–1912. Experiment No. 12. Surgical Pathology, No. 1997. Operation, March 25, 1912. Routine operation. On April 1 the dog jumped off a table and broke his leg. April 8 an attempt was made to get some callous cells to grow *in vitro*, and the leg was amputated at the fracture line. The transplants did not show any growth; a small

spicule of bone with surrounding callous was taken for microscopic section.

Microscopic Examination (Fig. 13). Under low power the specimen looks like a lace curtain, the darker perivascular areas being the calcium deposits while the lighter areas are granulation tissue and bloodvessels. This arrangement is clearly shown under high power.



FIG. 12.—Surgical pathology, No. 1907, under high power. Transition of connective tissue into fibrocartilage. A, fibrous connective tissue; B, fibrocartilage.

Dog No. 117. Surgical Research Series, 1912–1913. Experiment No. 28. Surgical Pathology, No. 2250. Operation, November 25, 1912. Cavity made in usual manner. Wound healed by first intention. On December 10 the dog jumped off a chair and fractured his humerus. Animal killed with chloroform on December 27. Duration, seventeen days.

Autopsy. There is considerable callous formation around the broken ends. No union has occurred, as there is a definite false point of motion, with over-riding of the fragments. Leg hardened

in formalin. Cross-sections taken through broken ends of the bone, including callus and surrounding connective tissue.

Microscopic Examination (Fig. 14). Around the periphery of the shaft there is proliferating new-bone formation. It is impossible to make out periosteum, as it fuses with the general connective-tissue infiltration. Surrounding the callus and new-bone formation is a fibrous tissue stroma. The loose ends of the bone are covered with tissue that resembles cartilage.



FIG. 13.—High power of surgical pathology, No. 1997. A, callous (new-forming bone); B, bloodvessels.

Beginning at the periphery there is a gradual transition from the surrounding connective tissue into fibrocartilage. Beyond the cartilage one sees strands of new-bone formation; there are places in this new bone where there are islands of cartilage cells; the cartilage cells become gradually smaller; their nuclei becomes irregular or stellate in shape, and their capsules gradually lose their blue stain and disappear, until there seems to be no definite dividing line between the cartilage and bone cells.

Dog No. 248. Surgical Research Series, 1912-1913. Experiment No. 36. Surgical Pathology, No. 2394. Operation, February 11, 1913. Upon attempting to make a cavity in the usual manner the leg was fractured. A Lane plate was applied, with fair approximation of the two ends; and wound was sutured and the leg put up in plaster of Paris.

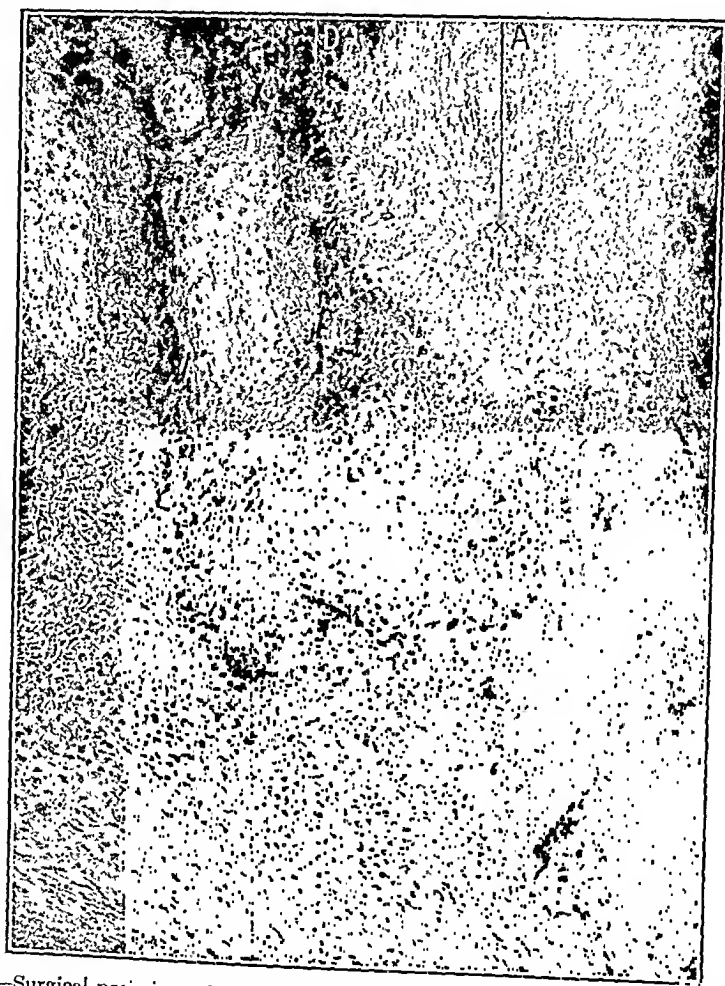


FIG. 14.—Surgical pathology, No. 2250. Repair of fracture. A, connective tissue; B, transition of connective tissue to osteogenetic cells; C, new bone; D, cartilage cells embedded in bone.

March 4 the cast was removed; wound healed. There was, however, no union, so the dog was killed with chloroform. Duration since fracture, twenty-two days.

Autopsy. The ends of the bone are thickened and club-shaped, and have considerable callus around them. Longitudinal sections made through the ends of the bone.

Microscopic Examination (Fig. 15). Here under high power one sees again gradations between connective tissue, cartilage, and bone.

CONCLUSIONS. In this series of experiments two types of repair of the bone have been observed:

1. Where the periosteum has been well stripped off the bone for a distance of several centimeters it is separated from it by serosanguinous fluid. Here the bone has apparently been repaired from the medullary cavity by a framework of connective tissue, upon which calcium salts have been deposited, forming osteoid tissue; there has also been a reparative process from the connective tissue of the Haversian canals at the sides of the bone incision.



FIG. 15.—Surgical pathology, No. 2394. Repair of fracture, under high power. A, cartilage; B, bone.

2. Where the bone has repaired under a definite fibrous connective-tissue capsule, which is continuous with periosteum and also adherent to the surrounding muscles. This connective tissue is apparently not different from other connective tissue, except that in immediate approximation to the newly forming bone there is a single layer of cells which are larger in shape and have nuclei that take a heavy stain. In places there is a metaplasia from the connective-tissue cells to these osteogenetic cells.

In the process of repair in fractures by the output of callus there is a metaplasia from connective tissue which seems to arise from the surrounding tissues rather than being a direct continuation of the

periosteum. There is also a direct metaplasia from a tissue closely resembling fibrocartilage into young bone.

In attempting to draw clinical deductions from these experiments in regard to transplantation of bone, it is reasonable to assume that the periosteum acts as a limiting membrane to the bone, tends to conserve its shape, and to furnish its blood-supply. If the periosteum is stripped from the bone of the transplanted part, numerous thrombi will occur, where the vessels enter the diaphysis; but if the periosteum is left attached, the blood-supply will probably be more quickly established through the vessels of the periosteum.

If small pieces of bone are transplanted, it is obvious that Haversian canals must be cut in many directions, thus allowing easy ingress to the newly forming bloodvessels. The fragments also must receive a good blood-supply from the entire periphery. They grow in this case without the aid of periosteum.

I wish to extend my thanks to Drs. Clarke, Auchincloss, and Prime for many kind suggestions and valuable advice, and to Dr. McWhorter and Mr. Agnew for making the photomicrographs.

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DIABETES MELLITUS AND ITS DIFFERENTIATION FROM ALIMENTARY GLYCOSURIA.

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TEN years ago anyone whose urine reduced Fehling's copper solution on boiling was considered to be suffering from diabetes mellitus, and the patient was directed by the attending physician to regulate his earthly affairs and prepare for death at any moment. So many of these individuals were seen to outlive all expectations, and finally to show no sugar whatever in their urines, that it led to a more thorough study and understanding of the condition. To the work of von Noorden,¹ with his oatmeal diet, more than to anyone else is due the credit of first establishing a scientific therapy for such; while Opie,² Mohr,³ von Mering and Minkowski,⁴ Lusk,⁵ and others have given us a deeper insight into the pathology of the disease. Opie⁶ has shown that in the majority of cases there is a degeneration of the cells in the islands of Langerhans in the pancreas, with atrophy of same. While there is no doubt that pathological changes in the pancreas will cause glycosuria, the writer has seen fatal cases of diabetes in which no pathological changes could be demonstrated in this organ, but in which they seemed to be limited to the liver, while other cases are reported in which no lesions whatever could be demonstrated. We must, therefore, content ourselves with a meager knowledge of the pathology of this disease and turn to physiology to explain many of the phenomena observed.

The various changes through which the carbohydrates pass before final utilization by the tissues as fuel is shown in the accompanying table.

Von Noorden⁷ believes that the pancreas through its hormone inhibits the liver in its normal tendency to part with its glycogen, and that failure of this action results in a hyperglycemia from overproduction of glucose. He does not think there is any lack of ability in the tissues to utilize the glucose in the blood. However, the recent experiments of Knowlton and Starling⁸ would tend to disprove this latter idea, and show that the pancreas while it does

¹ Metabolism and Practical Medicine, Chicago Med. Book Co., 1907.

² Jour. Exper. Med., 1901, v, 527; Johns Hopkins Hosp. Bull., 1901, xii, 263; Disease of the Pancreas, Philadelphia, 1910.

³ Sammlung klin. Abhandlungen über Path. u. Ther. der Stoffwechsel u. Ernährungsstörungen, H. 4, Aug. Hirschwald, Berlin, 1904.

⁴ Arch. f. exper. Path. u. Pharm., 1890, xxvi, 371.

⁵ Science of Nutrition, Philadelphia, 1909.

⁶ New Aspects of Diabetes Mellitus, New York, 1912.

⁷ Jour. Phys., No. 3, xlv, 162.

⁸ Loc. cit.

have an influence on the glycogenic function of the liver most certainly has a decided influence on the utilization of glucose by the tissues. The main point to bear in mind from a clinical standpoint is that whenever the normal glucose content of the blood (that is, 0.09 per cent.) is exceeded, the kidneys will excrete the excess and glucose will appear in the urine. It has been thoroughly accepted that the pancreas secretes a hormone which is absorbed by the blood and in some way presides over the glycogenic function of the liver.

Food substance.	In alimentary canal split up into:	Absorbed by portal system and transformed by liver into:	Stored up in muscles as:	Burned up by tissues into:	Remarks.
Saccharose, $C_{12}H_{22}O_{11}$.	Dextrose, $C_6H_{12}O_6$, and Levulose, $C_6H_{12}O_6$.	Glycogen, $C_6H_{10}O_5$. Glycogen.	Glycogen. Glycogen.	CO_2 and H_2O glycuronic acid. CO_2 and H_2O glycuronic acid.	Dextrose and levulose are excreted by the kidneys if not utilized by the tissues.
Starch, $C_6H_{10}O_5$.	Dextrose.	Glycogen.	Glycogen.	CO_2 and H_2O glycuronic acid.	
Maltose, $C_{12}H_{22}O_{11}$.	Dextrose, $C_6H_{12}O_6$.	Glycogen.	Glycogen.	CO_2 and H_2O glycuronic acid.	Excess maltose excreted by kidneys.
Lactose, $C_{12}H_{22}O_{11}$.	Dextrose and galactose.	Glycogen.	Glycogen.	CO_2 and H_2O .	When liver is deranged, galactose appears in urine.
Cellulose, $C_6H_{10}O_5$.	Very little if any effect in human.				
Proteids.	Peptones, amino-acids, xanthine bases. Ammonia. Toxic amines from intestinal putrefaction.	Serum, albumin, and globulin. Urea. Non-toxic compounds.	Syntonin, creatin, etc. Creatin. Creatin.	Urea, uric acid, glycol, and dextrose.	If liver function is deranged, have lowered alkalinity of blood.
Fats.	Absorbed through lacteals and into general circulation through the liver. Do not pass through the liver. Incomplete combustion results in diacetic acid.				

Anything affecting the cycle between the liver and the pancreas will result in glycosuria, or anything causing a rapid rise of the dextrose in the general circulation will cause a glycosuria, maltosuria, or galactosuria, depending in great part upon the particular carbohydrate eaten. Patients partaking of large amounts of milk often show a reduction of Fehling's solution, not because they have a true diabetes, but because their normal liver function has been overtaxed, with consequent chronic passive congestion of this organ, so that it is unable to transform into glycogen the galactose formed from the lactose in the milk. A liter (one quart) of milk yields about 48 grams of lactose, which is split up into 24 grams of

dextrose and 24 grams of galactose. The latter is differentiated from the former by its failure to ferment with a pure culture of *Saccharomyces Ludwigii* and its action on polarized light, while both reduce Fehling's solution. In hepatic insufficiency the liver is able to transform the dextrose into glycogen, but has lost this power for galactose. So constantly is this the case that the ingestion of 40 grams of lactose on an empty stomach, with a subsequent determination of the amount of galactose in the urine for four to six hours is universally adopted in the German and Austrian clinics as a test for liver function. This is an example of what one would regard as an "alimentary glycosuria," although glucose is not the sugar present.

Another type of alimentary glycosuria is exemplified by a case recently referred to me as a case of diabetes mellitus:

CASE I.—R. P., wholesale grocer, had suffered some prostatic trouble, and in the routine examination of his urine, by Drs. Hume and Logan, a heavy reduction of Fehling's solution was obtained, and he was referred to me. There was no thirst, no loss of weight, nor nervous manifestations of diabetes, and his urine was inactive to polarized light, yielding 7 per cent. calculated dextrose by reduction. Urine fermented by yeast. There was no diacetic acid or acetone. Specific gravity, 1.028, with a heavy reaction for indican. He gave a history of eating large amounts of sugar during the day, as he made a practice of grabbing a handful every time he passed the open sugar barrel in his warehouse. His liver dulness was increased to 14 cm., but otherwise all his organs were normal. On account of the failure in action to polarized light, it was evident that there was not a simple glycosuria, and inasmuch as the reduction ceased on the second day after his arrival in New Orleans, I concluded that it was a glycoleucosuria, due to the rapid absorption of the dextrose and levulose formed from the cane-sugar, with insufficient action of the liver and prompt excretion of both saccharides by the kidneys, together with some glycuronic acid.

He was put upon a low proteid diet to rest up the liver. No sugar was allowed, but glutinous substances and vegetables were given, while his liver function was stimulated by an initial calomel purge and a two weeks' stay at one of the spring resorts, whose water is rich in phosphate and sulphate of soda. On his return his liver dulness had diminished to 8 cm., there was no reduction with Fehling's solution, and after taking 100 grams of lactose on an empty stomach no galactose could be detected in the urine.

He went home happy in the thought that he had been cured of diabetes, but, fortunately, he never had a true diabetes, but had a simple alimentary glycosuria from insufficient liver action and an overindulgence in cane-sugar. Such cases as this von Noorden classes as prediabetic, and yet "they may go for a lifetime and never develop a true diabetes."

In diabetes mellitus there is a failure of the entire body to utilize not only the dextrose of the circulating blood, but there is a predilection for fat and proteid as fuel in preference to carbohydrate, with subsequent formation of beta-oxybutyric acid, acetone, diacetic acid, etc., from incomplete combustion of these foodstuffs. That incomplete combustion of proteids, or their excessive putrefaction in the intestines, can cause an acid condition in the blood identical with that seen in diabetic coma, I am firmly convinced, although I am not in accord with modern text-books on this point. Diacetic acid, acetone, and beta-oxybutyric acid are not particularly toxic, and I have seen fatal cases of diabetic coma whose urines just previous to death showed very little of these substances, but which were loaded with the products of intestinal putrefaction. Most practitioners make the mistake of considering the carbohydrate metabolism and not paying any attention to the proteid metabolism.

The following case shows the importance of a consideration of the latter:

CASE II.—L. N., white male, aged fifty years, manager of a saw mill, was referred to me by Dr. Picard on May 20, 1912, complaining of drowsiness, occasional headaches, with excessive thirst and ravenous appetite. Other than an attack of lobar pneumonia, twelve years before, he had never had a day's illness until 1905, when he consulted Dr. Picard for retention of urine, which was very abundant. Dr. Picard informs me that at this time he had vague abdominal pains and crampy pains in the limbs, and that his urine showed 2-per cent. of glucose. He had been getting along very well until ten days previous to his visit to me, when he had a sudden attack of nausea and vomiting, succeeded by a constant drowsiness and inability to remain awake sufficiently to attend to his business. He had been losing weight steadily for the past four years, but during the past ten days he had lost nearly twenty pounds.

Examination revealed a robust, ruddy individual, with all organs apparently normal, with the exception of a hypertrophied heart and a general emphysema. There was only moderate peripheral arteriosclerosis, and examination of the fundi showed both disks normal, with no pathological changes in the retina. Examination of his urine showed: specific gravity, 1.040; acid; 1.5 per cent. glucose by polariscope; large amount of albumin; great excess of indican and diacetic acid; negative urobilinogen; a few hyaline casts.

He was sent to Touro Infirmary, and was put upon Vichy and large amounts of bicarbonate of soda. A purgative of calomel, phenolphthalein, and rhubarb was administered, and a reduction in proteid food, with increase of carbohydrate food, instituted at once.

The following table shows his diet and the results of same:

Date.	C.e. urine passed in 24 hours.	Grams glucose in 24 hours.	Total calories.	Carbo-hydrate calories.	Calories lost in urine.	Per cent. calories lost in urine.	Weight, lbs.	Indian.	Remarks.
May 22	1280	28.1	1215	600	115.4	9.5	154	++++	Full proteid diet.
May 23	Lost	...	3175	1025	++	Full carbo-hydrate diet
May 24	2050	54.5	3825	1550	221.4	5.7	...	+	Oatmeal and corn-bread.
May 25	1570	35.8	3125	1440	146.7	4.5	...	0	Oatmeal and corn-bread.
May 26	1650	33.0	2450	775	135.3	5.5	155	0	Oatmeal and corn-bread.
May 27	1600	39.3	2500	1250	143.4	5.5	...	0	Macaroni.
May 28	2040	36.1	2525	1125	148.0	5.8	156	0	Oatmeal.
May 29	1650	25.1	2475	1150	103.2	4.1	...	+	Macaroni.
May 30	1760	35.2	2675	1075	144.3	5.4	...	0	Rice and potatoes.
May 31	1700	41.8	2675	975	172.0	6.4	...	0	Rice and potatoes.
June 1	1760	37.4	3475	1325	153.6	4.4	...	0	Oatmeal.
June 2	1170	37.1	4200	2850	152.3	3.6	159	0	Oatmeal and corn-bread.

He left the infirmary in two weeks, a changed man; his mind perfectly clear, no headaches, and an increase in weight of five pounds. I have heard from him at intervals of from three to four weeks, and he has continued to improve on a liberal carbohydrate diet. His urine contains 3 per cent. of sugar still, but there is no albumin and no diacetic acid, and he is to all intents and purposes a well man. He is able to assimilate oatmeal, corn-bread, and macaroni, as well as large amounts of fruit, but he cannot metabolize saccharose, rice, and potatoes.

It must be borne in mind that approximately 50 per cent. of the proteid molecule is transformed into glucose in the body metabolism, and that for every 1 gram of nitrogen in the urine, 5 grams of glucose are either burned up by the tissues or excreted by the kidneys, so that in endeavoring to rid the urine of sugar one must take this fact into account. It has been my experience, (and upon this fact also depends the good results of the von Noorden "Hafer Kur") that the excretion of sugar may increase for a short while after giving carbohydrates, but even during this greater excretion of glucose a greater percentage is utilized by the tissues. This is well exemplified in the diet table accompanying Case II.

It is not the purpose of this paper to consider all of the many points in physiological chemistry involved in a consideration of diabetes, but merely to call attention again to the fact generally accepted that complete withdrawal of carbohydrate food from a diabetic for a long period of time, invariably results in an acidemia, commonly spoken of as diabetic coma, in which beta-oxybutyric acid, diacetic acid, and acetone are usually found in the urine. It is also well to again mention that in the metabolism of proteids,

approximately 50 per cent. of the proteid molecule is split off as a carbohydrate radical, and that this accounts for the continued presence of dextrose in the urine even after complete withdrawal of all carbohydrate food. Dextrose itself is relatively non-poisonous in comparison to the other cleavage products of proteids, and before outlining a diet a consideration of the cleavage products of proteids should be considered, even more than those of carbohydrates.

The amount of glucose excreted by the kidneys is of far less importance than a consideration of the amount of diacetic acid, beta-oxybutyric acid, acetone, and indican. In referring to the tabulated chart of Case II, it will be noticed that on days of carbohydrate feeding, while he excreted a larger amount of glucose, the percentage of wasted calories compared to that ingested was progressively less, while he gained steadily in weight and all symptoms disappeared.

In the treatment of diabetes, drugs or proprietary medicine are of no benefit, if we are to judge by published reports, and the treatment resolves itself into a regulation of the patient's diet and personal hygiene, so as to avoid acidemia, which, however, when present, can be relieved by drug therapy. In overcoming the tendency to intestinal toxemia the writer has experienced good results from the administration of massive doses of cultures of the *Bacillus bulgaricus*, but the number of cases are as yet too few to draw any conclusions. Since Knowlton and Starling's⁹ article, we have administered 10 to 20 grains of an active extract of pancreas, every four hours on an empty stomach, with decided and rapid reduction, and even complete absence of glucose in the urine in two cases of diabetes, while in two others there was apparently no effect.¹⁰

Therapy along this line should, theoretically, yield good results, but the difficulty of obtaining absorption of the pancreatic hormone before it can be destroyed by the gastric juice will always remain a difficult problem. It is to be hoped that in the near future this hormone can be isolated and preserved in such a manner that it can be administered hypodermically, when the ideal drug for the disease will have been found. Until then, strict regulation of the diet will have to be relied upon, and for successful results one must consider the proteid metabolism, as well as the carbohydrate metabolism, and be ever mindful of the physiology underlying the condition.

⁹ Loc. cit.

¹⁰ Eustis. Acidosis, New Orleans Med. and Surg. Jour., September, 1913, vol. lxvi.

CHLOROMA, WITH REPORT OF A CASE OF THE MYELOID VARIETY.

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THE uncertainty that exists in the classification of a group of diseases of which the above title represents one, is such as to demand that all these be published, with the hope of ultimate clarification of our knowledge.

In the following report, one of us (F. X. W.) is responsible for the clinical observations, and the other for the pathological study, which was undertaken while the latter was a member of the department of pathology, of the Northwestern University Medical School. It is our desire, therefore, to express our obligations to this department, and especially to Professor F. R. Zeit, who furnished valuable suggestions.

SYNOPSIS. Clinical. Five-year-old white male; entire illness three months; proptosis and tumors about face; general glandular hyperplasia; gingivitis and necrotic pharyngitis, blood; moderate anemia; leukocytes, 9000 to 12,000, 80 per cent. of which were mononuclear, 4 per cent. of total were myelocytes, and a smaller number were myeloblasts; spleen and liver markedly enlarged.

Pathological. Chloroma deposits found in following locations: orbits, in frontal bones (sinuses, etc.), in temporal bone, on external surface of parietal bones, attached to cerebral and spinal dura mater, kidney, liver, and posterior surface of sternum. Eosinophilic mononuclear cells were found in some of the chloroma masses.

Clinical Data in Detail. C. M. R., white, male, aged five years, was brought to Wesley Hospital July 10, 1906. The child having been cared for in a public institution, the exact time of onset is unknown, but probably was six or eight weeks before admission to the hospital, the child at this time having just recovered from pneumonia. The first indication of illness was swelling between the eyes and at the angles of the jaw. There has been a gradual increase in the size of the swellings and a gradually increasing depression of spirits. Sleep has been troubled, and the facial expression has indicated some pain. Ten days before admission, stomatitis with bleeding gums was noted.

Previous Illness. Uneventful attacks of measles and chickenpox. Pneumonia just before onset of present trouble.

Family History. Mother is in an insane asylum on account of dementia following a puerperal infection. Parental lues denied.

EXAMINATION, July 31. General. Nutrition somewhat poor. Extremities slightly bluish. Eyelids dark bluish red, firm; pit slightly on pressure; otherwise no edema, except over forehead, where it is slight. Lips are a trifle cyanotic. Subcutaneous veins are prominent over both temporal regions, and extend forward onto brow.



FIG. 1.—Chloroma. Shows tumor of glabella and spongy gums.

Head. There is a large protuberance between the eyes and extending to the brow. This tumor seems to push apart the two halves of the face. The distance from one inner canthus to the other is 3 cm. The mass is quite hard, but softer than bone. There is a similar hard, dome-shaped mass 5.5 cm. in diameter in the right temporal region. This mass is smooth, not nodular, and harder than the one on the face. There is a similar swelling about 2.5 to 3 cm. in diameter in the left temporal region. The eyes are prominent, and seem to bulge from their sockets. Conjunctivæ (bulbar and palpebral) much injected. Eyes water. Pupils moderately dilated and react normally. No extrinsic paralysis. There is a thin frothy discharge from both nostrils. Mucous membrane of left naris injected. Slight abrasion at mucocutaneous junction. Mouth exhibits extensive inflammation of both gums, with ulceration. Tendency to bleeding. Foul odor. Teeth slightly loosened, but no evidence of decay. Tongue slightly coated. Pharynx injected and edematous. Tonsils not visible.

Facies. Pathetic. Voice thick. Marked coryza.

Neck. Lymphatic glands beneath right ear enlarged. They are freely movable and somewhat sensitive. Considerable number of pea-sized glands beneath the jaw. Anterior and posterior cervical glands enlarged and hard. Same true of axillary and inguinal groups. Epitrochlear glands are the size of small shot.

Thorax. Negative.

Abdomen. Slightly prominent. Lower pole of spleen on the level of the umbilicus, and its right border extends to the rectus muscle. Notch distinctly palpable.

Liver. Extends 7 cm. below costal arch.

Progress of the Disease. The symptoms, including the facial distortion, proptosis, conjunctival injection, became gradually more pronounced. The child became thinner, paler, more peevish and irritable, and complained of pains in the head. Pupils became slightly unequal. During the last week of life, fever was almost constantly present, being nearly always over 101°. Although the roots of the teeth became bare, the latter were not markedly loose. The pharynx presented a dark, gangrenous appearance; several gangrenous masses of almost unendurable odor were expelled during the act of coughing on the day before death. Manipulation of the mouth caused free hemorrhage. During the last week of life there was a noticeable diminution in size of all the swellings about the head. The mass between the eyes, in addition to diminishing in size, became somewhat softer. The face, however, has an appearance similar to that seen three or four weeks previously, although eyes project to less extent. (The diminution in the size of the swellings, etc., occurred during the administration of potassium iodide.) The child grew steadily worse, but was able to sit up and even to walk up to the last day.

August 14, 1906, the patient died quietly and without warning.

Blood Examination. (The following represents a synopsis of fourteen examinations made between July 12, 1906, and August 11, 1906, inclusive:)

Erythrocytes	3,300,000	to 2,400,000
Leukocytes	9,400	to 12,000
Hemoglobin	50 per cent.	to 60 per cent.

Differential count of leukocytes:

Polymorphonuclear neutrophiles	18.0 per cent.
Lymphocytes	60.0 "
Large mononuclears	16.0 "
Polymorphonuclear eosinophiles7 "
Myelocytes	4.0 "
Myeloblasts	1.3 "

The myelocytes have a diameter of about 15 μ . The cells, few in number, called myeloblasts by some writers, measure about 18 μ . They represent an early or embryonic stage of the myelocyte.

The erythrocytes exhibit some lack of uniformity in size, there being a fair number of microcytes and megalocytes. No polychromatophilia. No nucleated reds. In general they are well stained; a few cells, however, were pale.

Pathological Findings. In the following notes the microscopic findings accompany the postmortem description of each organ. The microscopic description of the chloroma mass in the orbit, the bone-marrow, etc., is reserved for the end of this section.

The autopsy was held in the morgue of Wesley Hospital, a few hours after death.

The body is that of a male child, 102 cm. in length. There is a swelling in the frontonasal region circular in outline and measuring 3.5 to 4 cm. in diameter; it is firmly adherent to the bone. A mass of lymph glands was found in the inframandibular region of each side. The chain of posterior cervical glands enlarged. On vertex of head is seen a mass similar to one in frontonasal region, but slightly smaller.

Head. On removing the scalp, there is seen on right and left temporal regions and extending to coronal suture a greenish substance not readily removed. The internal aspect of the calvarium exhibits in the frontal and parietal regions a similar material. The bone is rough and shows spicules. Both retrobulbar spaces are filled with a soft, greenish material. The same material is found in the left temporal bone (petrous portion), but not in right, and also in the frontal sinuses. The dura mater exhibits on its outer aspect the same greenish material, which at one place has broken through so as to appear on the inner surface of the membrane. Between the spinal dura and the vertebræ is found a greenish substance similar to that found in the head. At the level of the seventh cervical vertebra it forms a tumor-like mass the size of a navy bean.

Brain. Weighs 1152 gm. Externally and on section negative.

Spinal Cord. Grossly and microscopically no changes.

Larynx. The upper part of the larynx shows necrosis, as does also the epiglottis and the fauces. The nasopharynx exhibits necrotic masses, which on microscopic section show complete necrosis of the mucosa and submucosa and of some of the layers of striped muscle. Between the bundles of muscle fibers and even between the individual fibers are seen mononuclear cells, some of which are ordinary lymphocytes, but many of them are larger cells supplied with large, pale nuclei.

Thorax. Attached to the internal aspect of the sternum at the junction of the manubrium with the gladiolus is what appears to be a lymph gland. On section this material has a microscopic structure, almost identical with the orbital tumor, although a moderate number of spindle cells is seen. The right pleural cavity exhibits a few easily torn adhesions.

Lungs. The left lung weighs 162 gm. Floats high in water. Pale in color. Numerous split-pica-size purple areas firm to touch. The right lung weighs 176 gm. Also floats high. Areas as in other lung, containing little or no air. Fibrous adhesions obliterate the fissure between the upper and middle lobes. Cutting into the anterior part of the lung, pus is found in the bronchi, also what appears to be inflammatory tissue is seen. The small, airless areas in each lung exhibit microscopically the following: Some of the alveoli are filled with serum, but for the greater part they are filled completely with cells without being accompanied by an appreciable amount of fibrin. In some areas there are a few polymorphonuclear cells; the vast majority of the cells, however, are mononuclear. Some of these (in some areas a considerable number) resemble the lymphocyte; however, in the majority of areas examined the preponderance of cells is represented by a cell with a chromatin-poor nucleus. Also, this same infiltrate is seen in the alveolar walls. In many places, where the infiltrate is marked, it is impossible to distinguish the alveolar walls. The anterior portion of the right lung mentioned above as containing pus, etc., exhibits microscopically the following: A massive infiltration is found, the greater part being found in the wall of and surrounding a large bronchiole, part of whose epithelial lining is missing. In the infiltrate are found a moderate number of thin-walled vessels. Although the infiltrate contains a considerable number of cells, with poorly stained nuclei, a much greater proportion (than in small areas mentioned above) are seen approaching the adult type of cell, especially the lymphocyte. The polymorphonuclear leukocyte is present, but not in great numbers. A few eosinophilic mononuclear and polymorphonuclear cells are seen. We interpret the above findings to indicate an invasion of the lungs by the same cells as are found elsewhere. There has been some inflammatory reaction to this. The pus in the bronchiole is due either to breaking down and infection of a chloroma infiltrate (as seen in the pharynx), or possibly to the occlusion of the bronchiole followed by infection, due to the pressure of the infiltrate.

Heart. Weighs 94 gm. Myocardium somewhat pale. Valves normal. Microscopically, no marked changes.

Lymph Glands. The lymph glands at the bifurcation of the trachea are markedly enlarged; some of them are as large as hickory nuts. On section they are pale and show no caseation.

Abdomen. Cavity is dry.

Liver. Greatly enlarged and extends in right mammary line 12 cm. below the costal arch, and in median line 14 cm. below the ensiform. Weighs 947 gm. Dimensions: 19 x 16 x 11 x 7 x 4.5 cm. The enlargement of the organ affects mainly the right lobe. At the hilum several large glands are found. The organ on section presents a pale appearance and the markings are less distinct than

normal. Microscopically, in the portal territories are found moderately extensive infiltrations of cells of which each has a single nucleus. These nuclei in some cases are deeply stained, and in others have a vesicular appearance. These cells correspond fairly well in size to those seen in the retrobulbar masses. Similar cells are seen between the columns of liver cells. Otherwise the organ appears normal.

Spleen. The spleen is greatly enlarged, extending 7 cm. below the costal arch in the anterior axillary line. Weight is 231 gm., and dimensions 14 x 8.5 x 4 cm. Near upper pole, fibrous tags are seen. The color is uniformly pale and the markings are less distinct than normal. On microscopic examination the Malpighian bodies are much less distinct than normal. The cells of the pulp are mononuclear, and vary in size from the dimensions of the ordinary lymphocyte up to diameters of 10μ or more. In general the larger cells have nuclei which are less deeply stained. A few cells having a diameter of about 20μ , and containing 3 to 5 nuclei, are found. A considerable number of mononuclear cells are found with eosinophilic granules. These cells measure about 10μ in diameter and their nuclei take a moderately deep stain.

Kidneys. The right kidney weighs 72 gm.; appears pale. Capsule strips readily. Markings are fairly distinct. The ratio of cortex to medulla is 1:2. The cortex contains a white nodule as large as a pinhead. The left kidney weighs 75 gm. The cortex contains a greenish-white mass surrounded by a hyperemic zone. This mass, measuring about 1 cm. in diameter, appears on section somewhat wedge-shaped, with the base at the surface of the organ; otherwise the description of the right kidney applies. Microscopically, the kidneys show the following: "The epithelium of the convoluted tubules seem slightly lower than normal. Some of the nuclei of these cells take the stain poorly and in some the nuclei cannot be found. The capsule of Bowman exhibits some distention; however, no evidence of abnormal contents is seen. The pinhead-sized nodule mentioned in the right kidney and the larger wedge-shaped area in the left have a similar structure, except that the latter has a somewhat looser texture, and one description, therefore, will apply to both. These masses, microscopically, do not have the sharp line of demarcation found in the ordinary neoplasm. The cells are supported by a delicate fibrous network. An occasional thin-walled vessel is seen in the midst of the cells, which are practically all mononuclear, only a few having two or three nuclei. No granules were seen. The diameters of the cells run up to 13 to 15μ , more of the cells in the nodule of the right kidney attaining this size than in the nodule of the left. The nuclei are in part poor in chromatin; other cells, however, exhibit nuclei with good staining powers. No cells resembling the ordinary small lymphocyte were seen.

The *mesenteric* and *lumbar glands* were all enlarged, reaching the size of split peas.

Pancreas. The *pancreas* weighs 40 gm., and shows no changes. *Stomach* and *Intestines* show no change.

Urinary bladder, no change.

Left adrenal, no changes (right not found).

Marrow. The *marrow* of the right femur has a greenish-reddish appearance.

MICROSCOPIC EXAMINATION OF MASSES IN ORBIT, ETC. *Retrobulbar tumor.* This is a mass of cells supported by a fine network of fibrous tissue. A moderate number of thin-walled vessels is seen. The cells are fairly large in type, about one-half of them measuring 10 to 12 μ in diameter. No polymorphonuclear leukocytes were found, the cells being all mononuclear, with the exception of a moderate number containing each two or three nuclei, possibly the result of subdivision. There is a moderate number of cells whose nuclei take the stain somewhat deeply, resembling lymphocytes. The majority of the cells, however, have rather large, more or less poorly stained nuclei, which are always surrounded by fair amounts of protoplasm, although the nucleus occupies more than one-half the diameter of the cell. The nuclei are round or oval. A very few eosinophilic mononuclears are seen.

The *tumor* in the *spinal canal* in general is the same as structure just described, there being, however, a slightly larger number of eosinophilic mononuclear cells.

The *mass* in *glabella* (the structure was decalcified) corresponds to the two tissues above described, containing, however, as does the mass from the spinal canal, a larger number of eosinophilic mononuclear cells than does that from the orbit.

The *tumor* from the *dura mater* has the same structure as the orbital mass.

Smears from *bone-marrow* (only the hematoxylin-eosin specimens were of value). Practically all the cells are mononuclear, only an occasional polymorphonuclear being seen. They range in size up to 18 μ , the large type predominating. The nuclei occupy the larger part of the cells, the protoplasm not being made out distinctly in most cases. The nuclei in appearance are midway between the embryonic and adult types. An occasional mononuclear cell with eosinophilic granules is seen. In the paraffin sections of the bone-marrow the cells correspond in a general way to those just described, although a large proportion of what appears to be small lymphocytes is seen. Also the nuclei throughout are more deeply stained.

PATHOLOGICAL DIAGNOSIS. Myeloid chloroma with deposits in the orbits, sinuses of the frontal bone, petrous portion of the temporal bone, external aspect of the parietal bones, on cerebral and spinal dura, in pharynx, lungs, kidneys, spleen, and liver.

Bone-marrow changes. Chronic diffuse nephritis of the parenchymatous type (moderate degree).

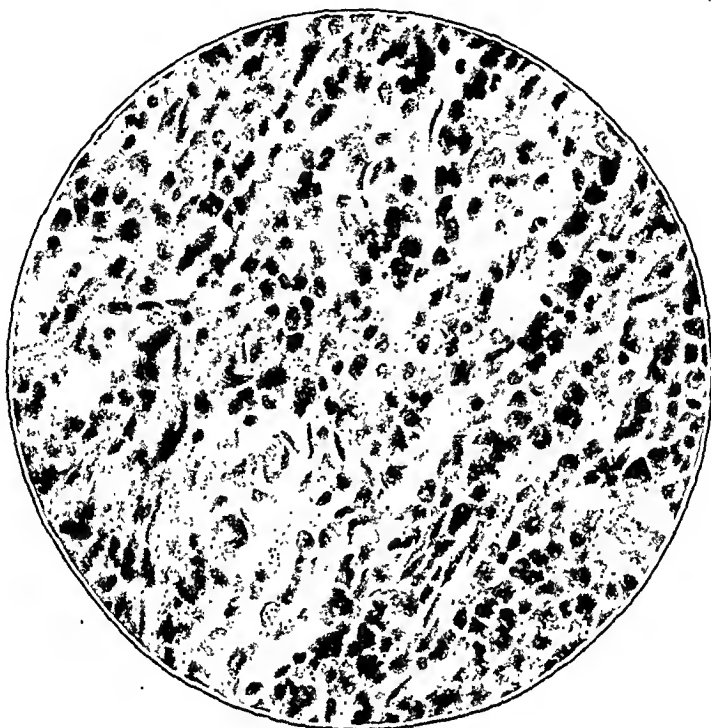


FIG. 2.—Chloroma. Tumor mass from orbit. $\times 350$.



FIG. 3.—Chloroma. Infiltration of right kidney. $\times 60$.

That we are dealing with a case of chloroma, there can be no doubt; and inasmuch as some myelocytes were found in the blood, and a moderate number of granular mononuclear cells in some of the tumor masses, we are justified in applying the term myeloid chloroma, which represents, judging from the cases published, the more uncommon form of the disease. It should be mentioned here that other cases of myeloid chloroma reported show a much larger proportion of myelocytes in the blood than does the case under consideration.

That chloroma is a disease of the blood-making organs, and not, as at one time supposed, a neoplasm ("green cancer") is practically undisputed. It would seem to fit in best with acute leukemia. Treadgold, in a masterful article, endeavors to point out, between the two conditions, certain differences which impress one as being differences of degree rather than of kind. Some authors, among whom are Treadgold and Dock and Warthin, state that the chloroma, compared with acute leukemia, exhibits greater malignancy; not so much, however, in its rapidity of growth as in its tendency of the cells to invade surrounding tissue, especially bone; and this is the reason that we observe, in the former disease, the cells leaving the bone-marrow and appearing beneath the periosteum. As suggested by Treadgold, the two diseases agree in the following: Age: average, seventeen to twenty years. Sex: males more frequently afflicted. Symptomatology: weakness, marked anemia, hemorrhagic tendency, splenic and glandular enlargements, deposits in the liver, kidneys, and less frequently lungs.

In chloroma, deposits occur commonly in the orbits, temporal region, and elsewhere in relation to the cranial bones; also in the prevertebral tissue, skin, and other locations (organs) where tissue analogous to that found in chloroma does not normally exist. However, non-chloromatous growths sometimes occur in these locations in association with lymphatic leukemia. In chloroma the cells are, on the whole, larger and possess more perinuclear protoplasm, not alone in the blood and bone-marrow, but also in the tissues. Treadgold believes, therefore, that the greater pathological malignancy may be accounted for by the additional quantity of protoplasm in the morbid cells increasing their ameboid powers.

Are we able to make a clinical diagnosis of chloroma? When we consider that at least two cases have been described (Birk, Leber), typical pictures of the disease without the lesions having a green color, we must answer this question in the negative. We must content ourselves with a diagnosis of acute leukemia. The more important clinical manifestation, aside from the blood changes, is the presence of tumor masses about the bones of the face; but this sign sometimes fails.

But sometimes we have evidence during life of invasion of the cranial bones without visible tumors being present. For example,

in Gumbel's case the patient, on account of involvement of the petrous portion of the temporal bone, suffered from disturbances of hearing. In the cases of v. Recklinghausen, Sternberg, Schmorl, Waldstein, Hitschmann, Türk, and Lenhdorff no evidence is furnished in the reports of invasion of the cranial bones. However, in a case of acute leukemia if we find evidence of masses in the orbits (proptosis), tumors about the glabella or in the temporal regions, we may reasonably expect to find these masses of a green color when the autopsy is performed.

But why be so concerned about a hair-splitting diagnosis? The more literature one reads concerning this class of diseases the more is he confused with the various terms used. It is quite well settled that acute lymphatic leukemia originates in the bone-marrow. The same is true of even chronic lymphatic leukemia, with few, if any, exceptions. The disease under consideration has the same point of origin. Therefore, when we compare chloroma, which is essentially acute, with other acute leukemias, one is not able at all times to draw hard and fast lines, especially if we ignore the green color, this being, of course, an autopsy finding. However, the tumors about the head, being the common thing in chloroma, and of infrequent occurrence in the other leukemias, are always indicative of an unusual type of leukemia. Summing up the whole situation, it seems that for an absolute diagnosis of chloroma we must depend upon the presence of the green color of the lesions at autopsy. The source of the color has always been an interesting question. Practically all authors agree that this disappears a short time after the body is opened. In our case we have an exception, inasmuch as the color persisted in preserving fluid (Kaiserling). In fact, even after a lapse of more than four and one-half years the masses in the dura mater, although somewhat darker in shade than at the time of the autopsy, were still distinctly greenish in tint. Ayers makes the following statement in regard to the specimen from his case: "On having placed the tumor in alcohol, the color disappeared entirely within twelve hours. On the other hand, the specimen kept within a tightly corked bottle, still retains the greenish color; in fact, the color has become even more intense." It is quite well settled that the color is not due to foreign pigment, such as iron. The consensus of opinion seems to indicate that it is something inherent in the cells of the tumor masses much the same as we have, in plants, green protoplasm (chlorophyl). Treadgold says in regard to the peculiar color: "We have already seen that abnormal myelocytes and myeloblasts are the pathogenic cells in chloroma and that green lesions never exist in pseudo-leukemia, lymphosarcoma, and acute lymphatic leukemia. Possibly a degeneration of the granules or perigranular protoplasm of these cells, or an abortive attempt to form granules is the real

source of the color, aided by the broken-down products of hemoglobin."

BLOOD FINDINGS IN CHLOROMA. The blood shows an anemia evidenced by a diminution in the number of erythrocytes and in the percentage of hemoglobin. Of course, the severity of the anemia in a given case will become more and more accentuated as the patient approaches his fatal termination. In the case of Pope and Reynolds, the erythrocytes numbered only 900,000 and the hemoglobin 25 per cent. In Türk's case the red cells went as low as 583,000, and the hemoglobin at one time 19 per cent. and later 14 per cent.

Sometimes nucleated erythrocytes are found; Sternberg reports not only normoblasts, but also some megaloblasts.

The leukocytes are usually increased in number, and may show a count of 300,000 or more. However, in the case of Lehdorff, published in 1910, the count was only 5100; in our case 12,000 was the highest count, while in Bramwell's case 13,000 was never exceeded. The number of leukocytes, therefore, is not of paramount importance. The significant finding is the presence of cells of embryonic type, cells from the bone-marrow that represent the forerunner of the myelocyte. These cells are sometimes called marrow cells ("Mark Zellen" of the Germans). Others use the term "myeloblast." The same cell is found, of course, in the blood of acute leukemia. In Buchanan's *The Blood in Health and Disease* an excellent chart is given showing the derivation of the leukocytes. In this the cell under consideration is called a non-granular myelocyte. It is a large, non-granular, mononuclear cell, with a nucleus more or less embryonic in type (pale) and occupying the larger part of the cell. In our case the embryonic type of cell forms a much smaller percentage, and the lymphocytes a larger percentage than is true of most cases of chloroma.

TWO VARIETIES OF CHLOROMA. This refers to the lymphoid and the myeloid types. The myeloid variety is supposed to bear to splenomyelogenous leukemia, the same relation as does the lymphoid type to lymphatic leukemia. Paulicek and Wutscher reported a case in which the patient, aged twenty-six years, was suffering from what was apparently an ordinary splenomyelogenous leukemia. After receiving x-ray treatment for one month, he was discharged from the hospital as improved. Five months later he returned, and his autopsy, at the end of a two months' stay in the hospital, showed chloroma. Roman furnished a list of the myeloid variety of chloroma previously reported. As previously mentioned, we believe that our case belongs in this group. In this type one should find myelocytes in the blood. At least some of the cases have exhibited in the chloroma masses, granular mononuclear cells, which of course will have to be grouped with the myelocytes. The myelocytes in the the blood may reach a high

percentage. Pope and Reynolds report 32 per cent. and Türk 47 per cent. It will be recalled that in the specimens from our case, we found cells with eosinophilic granules, as reported also in the case of Klein and Steinhaus.

COURSE. The disease runs a course lasting usually a few months (two to four). Some patients have lasted less than eight weeks. Others have run a longer course: Horing's case (seven months.) Huber's (over one year), Schmidt's (fifteen months), Dock's (one year). The disease is essentially fatal.

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A NEW METHOD OF GASTRIC TESTING, WITH A DESCRIPTION OF A METHOD FOR THE FRACTIONAL TESTING OF THE GASTRIC JUICE.

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PHILADELPHIA.

WHILE the passage of the stomach tube in the great majority of cases is an easy matter, it is questionable whether routine examina-

tion by this instrument is desirable. The average individual is willing to submit to almost any procedure when the condition of his digestion is such as to call for relief, but will hardly be in sympathy with such methods when his digestion is only temporarily deranged. Furthermore, while there are some authors, like Bourget, who consider that the stomach-tube has almost no contra-indications, there are others who find many conditions which might militate against its use. Needless to say, there are many occasions when we desire a sample of or information about the gastric juice without inconveniencing the patient, and it is toward the solution of this problem that I wish to report simple direct methods for the estimation of gastric juice. For years physicians have sought for some other method of examining the gastric contents than by the ordinary stomach-tube and the possible methods at our command may be enumerated as follows:

DIRECT METHODS. The most important of these is the Einhorn bucket. While I have not had any direct experience with this instrument, I have experimented with a bucket of similar shape and dimensions. It is true that it represents a possible method of examining the gastric contents, but it is by no means free from objections. Its construction is such as to permit the passage of pharyngeal and esophageal secretions in the superior orifice of the capsule, and even though precaution be taken to thoroughly gargle the throat, this by no means obviates the esophageal mucus which is called forth by the passage of the instrument.

The same thing may be said regarding the sponge and string method of Spallazani and Edinger. It is almost impossible to pull either the sponge or bucket up without encountering pharyngeal or esophageal secretions.

The use of the Dunham thread test and the recent gastrognost of Freidrick's is likewise open to the same objections, and I question whether the mottled staining of the latter, which its author details as characteristic of chronic gastritis, may not be due to its passage through the esophagus.

INDIRECT METHODS. It has been proposed to give bicarbonate and auscult for effervescence. Anyone who has had experience with this method knows how inconstant and unsatisfactory it is. It represents one of those methods which theoretically should be good, but which fail in practice. In many cases in which the bolus of food is more or less firm and free hydrochloric acid is undoubtedly present, but few crepitations are heard. To my mind its only value is in hypersecretion, where a continued shower of fine rales might suggest the condition. The use of the Leon Meunier ether capsule gives very irregular results, as I have frequently had occasion to witness.

I therefore conceived the idea of using a simple capsule which could be easily swallowed and withdrawn at any given interval.

In this capsule substances were placed capable of indicating the condition of the gastric juice. There was some difficulty in having such a capsule cut, but it was finally made of hard steel, plated with silver. Fig. 1 shows such an instrument in different sizes. It consists of two parts: the head perforated to permit the passage

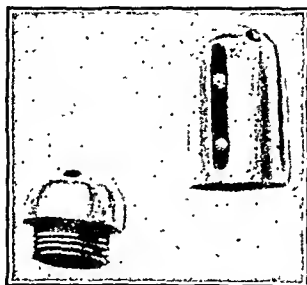


FIG. 1.—Enlarged view of capsule.

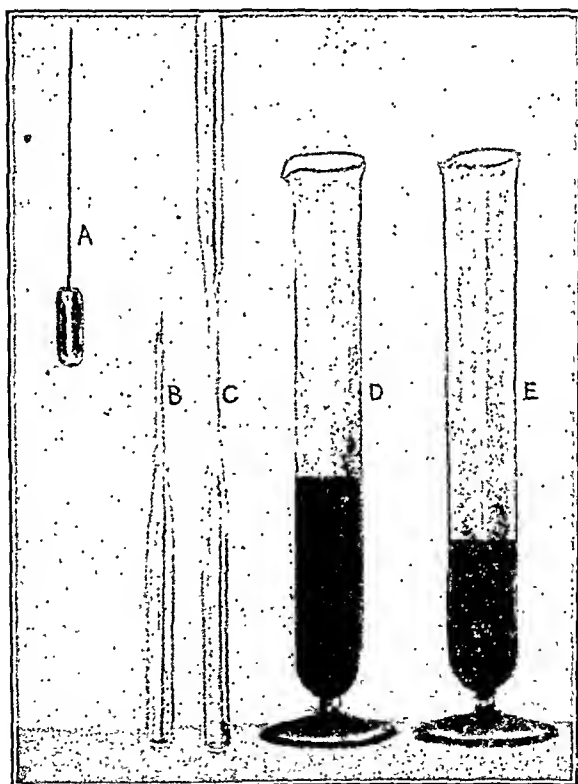


FIG. 2.—Material for preparing capsule.

of a small silk thread, and supplied with a screw thread, by which it is attached to the body. This is likewise perforated and slotted to permit of the greatest possible ingress of liquid.

In experimenting with indicators, I found the best possible base was one of agar-agar, which recommends itself, owing to its form

and consistence as well as its known refractivity to digestion. It is a very workable medium, and can be prepared in tubes like the various bacteriological media. It is best to use a 2.5 per cent. solution, as the addition of various coloring matters will soften it somewhat. Various substances were tried: Congo red, phenolphthalein diamidoazobenzol, litmus, of these only the first two gave appropriate media. I found, for instance, that while it was possible to prepare an excellent preparation of Congo red by adding a 1 per cent. aqueous solution of Congo red to the agar-agar jelly after it has cooled to 40° , the same solution added to hot agar-agar results in a precipitation of the dye, which is of little value. Usually it is well to see that the jelly is distinctly alkaline by adding a few drops of $\frac{n}{10}$ NaOH. When these precautions are observed, a clear red jelly is obtained. Phenolphthalein being soluble in

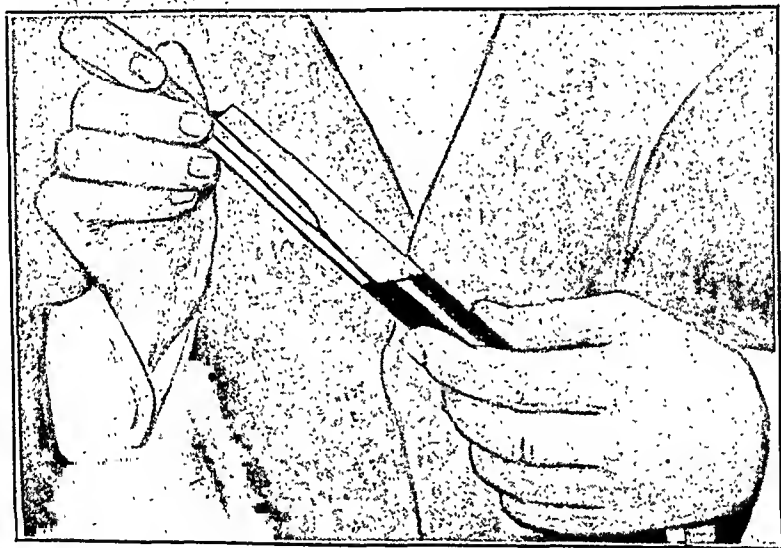


FIG. 3.—Method of introducing media into one of the pipettes.

alcoholic solutions is precipitated by agar-agar, but if some of the indicator solution is titrated with $\frac{n}{10}$ NaOH it is possible to obtain a transparent strongly colored alkaline solution, which can be fixed with the agar-agar medium at a low temperature and produces a brilliant crimson medium. Diamidoazobenzol is not susceptible to such preparation, inasmuch as it precipitates in the form of a bright yellow powder, which is apparently far less sensitive. Litmus, on the whole, is not soluble enough to yield sufficient color for this purpose, and the same may be said of alizarin. We have therefore in Congo red and phenolphthalein two indicators which are capable of demonstrating free acidity, and in the absence of the former, combined acidity. These media are prepared in tubes available at a moment's notice.

Various methods were tried: cubes of agar-agar, beads covered

with the jelly, strips saturated with the same combination, but it was finally decided that capillary tubes gave by far the best results.

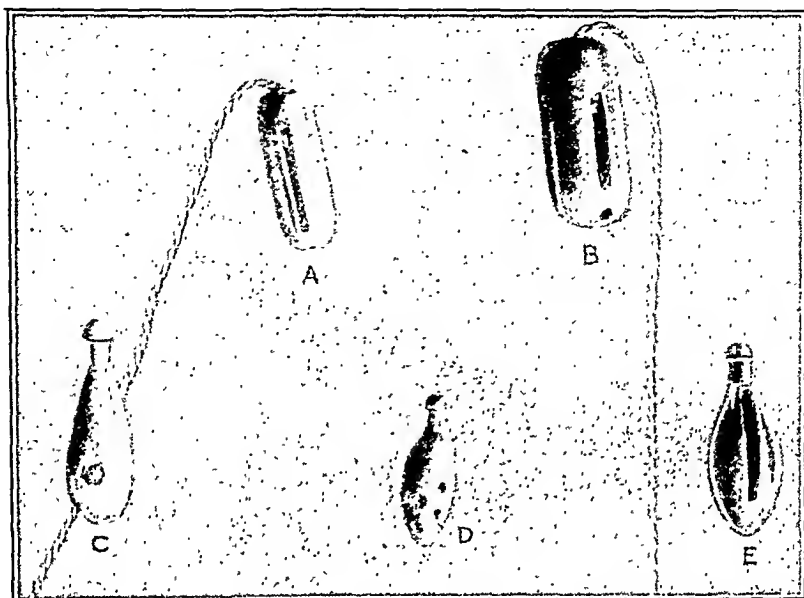


FIG. 4.—A, small capsule; B, large capsule; C, first tip constructed; D, Einhorn tip; E, modified tip.

These were prepared by drawing out ordinary glass tubing in the usual manner until the diameter approached 1.5 mm. These pipettes were then kept ready for use, and when it was desired to perform a test they were simply plunged into the jelly, withdrawn,

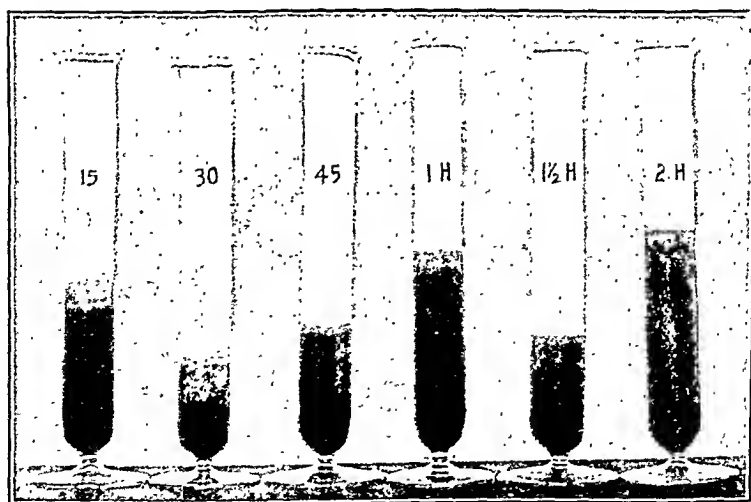


FIG. 5.—Fractional specimens obtained with tip.

and a core of the substance remained in the tube. Pieces were then cut off 8 mm. in length and inserted in the capsule. The capsule

was then given at any stage after a test meal or, for that matter, after an ordinary meal, swallowed in the usual manner, with a little water, and allowed to remain in the stomach ten to fifteen minutes and then withdrawn, taking the precaution to gell the patient to swallow when the capsule reaches the root of the tongue. I usually perform Mett's test *in vivo* by taking one of the capillary tubes, sucking up some fresh egg albumen, holding the pipette over a boiling-water bath for two minutes, which results in a softly coagulated albumen capable of showing peptic digestion. I have been able to demonstrate the digestion of more than 1 millimeter from either end in the course of an ordinary Ewald meal.

While experimenting in Paris with the Einhorn duodenal tube, I became convinced that if the tip was modified, it would be possible to obtain acceptable specimens of the gastric juice. Unfortunately, the tip was so constructed that the perforations, being very minute, became occluded with mucus or alimentary debris, resulting in a small foamy specimen insufficient for testing purposes. Palefski, recognizing the difficulties encountered in this tube, modified it so that the tip instead of weighing 48 grains as does the Einhorn instrument, weighed 105 grains. The great advantage, besides the fact that it could be more easily swallowed, was that it insured a more rapid passage into the duodenum. He used a gold-plated lead ball weighing 105 grains. The following is the table he gives regarding the relative merits of the three tips to which is appended the tip I am about to describe:

Substance:	Gross' perforated, calibrated, lead ball covered with tubing.	Einhorn's perforated brass capsule.	Palefski's perforated gold-plated lead ball.	Author's slotted steel or bronze silver-plated bulb.
Weight, grains . . .	160	48	105	90 to 120
Long axis, inches . . .	$\frac{5}{8}$	$\frac{7}{8}$	$\frac{3}{8}$	$\frac{7}{8}$
Size tubing . . .	20 French.	8 French.	8 French.	8 French.
Swallowing . . .	Difficult.	With water.	Easily.	Easily.
Reaches pylorus . . .	Few minutes. By gravity.	Indefinitely.		
Reaches duodenum	many hours?	1 to 2 hours	1 to 2 hours

The great advantage of the new tip is the fact that it is slotted instead of perforated, and the slots are so cut that *their diameter is as great as the caliber of the rubber tubing*, in that way assuring the more perfect aspiration of material. It is made of steel, or can be made of manganese bronze; is bulbous in shape, so as to be easily swallowed; weighs from 90 to 120 grains, depending on the extent of the slotting, and when linked with the customary No. 8 French tubing will not only serve as a most acceptable duodenal tube, but finds an even greater field in the study of the gastric contents, capable of being left in the stomach for long intervals, and enabling us to make a fractional study of the gastric juice over the whole period of digestion. The weight is sufficient to permit rapid swallow-

ing, at the same time assisting by gravity its passage through the duodenum. In fact, in making a gastric study, it is repeatedly necessary to caution the patient not to let the tube slip in beyond a certain point, owing to the tendency of the stomach to propel it toward the duodenum. I cannot say that the ordinary Einhorn tip requires as much time to enter the duodenum as the above table would indicate, but I know that there is no comparison between that tip and this one. It is possible in practically every case where no obstruction or lack of motor tone occurs, to enter the duodenum in less than two hours. In our gastric studies this factor must be controlled by regulating the amount of tubing swallowed. A further advantage of this tip is the fact that mucus and food debris as well as juice is extracted, and in this way it is possible to obtain a composite sample of the gastric contents, more than sufficient for testing purposes. I have on repeated occasions obtained twelve graded samples representing the entire cycle of gastric digestion in which some of the samples were 25 c.c. in amount, and none insufficient for quantitative testing purposes. This therefore represents a practical method of following the whole cycle of gastric digestion with a minimum of discomfort, *enabling us to construct a curve which graphically represents every phase*. It is likewise possible to perform lavage and inflation, and recently, on the principle of the stomach whistle, I have attempted to outline the stomach by ausculting the whistling sound which is heard when air is pumped through the tip. Furthermore, about a year ago I was enabled to obtain photographs on one case of the isolated duodenum by the injection of bismuth through the duodenal tube.

The advantages of the capsule are:

1. It offers us a method of inserting practically any substance whether indicators or substances to be digested into the stomach and to withdraw the same when desired.

2. This capsule can be swallowed at any stage in digestion and the condition of the gastric juice read off.

3. In no case have I seen any divergence from the results obtained by the titration of an ordinary Ewald meal, and in one case where both Ewald meal and capsule showed no free hydrochloric acid, the capsule on the same patient with a mixed diet showed a trace of this substance which was confirmed by subsequent examination.

4. Various substances, like meat, can be inserted into the capsule and gastric digestion observed.

5. It should be of value in determining the presence of an acid rest in the stomach. Its weight assisted by the swallowing of a little water will rapidly propel it to the bottom of the stomach and the possibility of gastrosuccorhea may be demonstrated.

6. The preparation of the indicator media is easy and requires no sterilization.

7. The size of the capsule is such that it can be swallowed by anyone with practically no discomfort, and even in infectious condition the condition of digestion can be recorded.

8. Although esophageal and pharyngeal secretions can penetrate the slots of the capsule, they can in no way vitiate the result, as they can act only on the extreme end of the capillary tubes, while in practically every instance the reaction takes up one-half of the tube or more.

It is hoped that further methods can be elaborated for the use of this capsule in the future.

Briefly the advantages of the modified tip and tube are:

1. It represents a practical method of fractional testing of gastric secretion, observing the entire cycle of gastric digestion, and following the transit through the duodenum.

2. By this method inflation and lavage can be performed and the organ delimited by auscultation as outlined above.

3. The great advantage of the present tip besides the fact that it embodies the weight and the form best suited for the purpose, is that its slotting is of such size and form as to represent the maximum caliber of the tubing and permit us to obtain a composite sample of the juice.

OSTEITIS DEFORMANS (PAGET) INVOLVING A SINGLE BONE: REPORT OF A CASE.

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OSTEITIS deformans (Paget) belongs to the rare affections of bone. Within recent years more interest has been taken in this malady, as is evidenced by the appearance in the literature of numerous case reports, some containing valuable additions to our knowledge of the pathogenesis of this disease.¹ Among the cases of osteitis deformans described in the literature there are instances in which the disease remained limited to one or two bones.² Some of these descriptions are accompanied by histological and radiographic studies, which make it fairly certain that they are genuine examples of Paget's disease, since the pathological changes observed in them correspond with those pictured by Paget³ and Butlin.

¹ Recently I had the opportunity to study six typical cases of Paget's disease admitted to the Johns Hopkins Hospital and Dispensary. Hurwitz, Johns Hopkins Hosp. Bull., September, 1913.

² The existence of such localized forms of hyperostosis has led some authors to regard leontiasis ossea (hyperostosis cranii) not as a separate disease entity, but as a form of osteitis deformans in which the morbid process is confined to the bones of the cranium. Prineas, Trans. Assoc. Amer. Phys., 1902, xvii, 386.

³ Med. Chir. Trans., 1877, lx, 37.

The following case record is of clinical interest, since radiographic study shows that in this patient the disease was limited to one bone, the right femur, although the malady lasted for about four or more years.

CASE (Disp. No. F. 9283).—J. M., white, aged fifty-six years. In July, 1913, the patient came to the Johns Hopkins Hospital dispensary complaining of pain in "both hips and in the small of the back."

Family History. There was no history of any unhealthy inheritance; the patient's father died of "Bright's disease" at the age of fifty-nine years; his mother died during childbirth. All of the members of his father's and his mother's family were well. The patient was not aware of the existence of tuberculosis, heart disease, cancer, rheumatism, nor gout in any members of his family; none of them had suffered from a similar malady. The patient has been married for twenty-five years; he had had two children, one son and one daughter; both of his children were well. His wife had one miscarriage twelve years before.

Personal History. The patient could not recall any diseases of childhood. He had always been a robust young man. At the age of eighteen years he had typhoid fever and "meningitis" (?); this illness lasted about three or four months and terminated uneventfully. When twenty-two years old he had a venereal sore, which lasted a few weeks and yielded to treatment; the exact nature of this lesion was not clear; there was no history of any secondary luetic manifestations. Five years later he had a gonorrheal infection. Fifteen or eighteen years before the patient was accidentally shot in the right leg; two bullets penetrated his body, one passing through the soft parts of the middle third of the right thigh and the other a little above this point. According to the statement of the patient's physician at that time the bullet did not penetrate the bone. After a few weeks' illness the patient recovered completely and no impairment of function of the limb followed this accident.

Present Illness. For thirty-five years the patient suffered from intermittent pain in the back. Except for this pain he considered himself well up to four years before, when he was fifty-two years old. At this time he began to complain of "rheumatism" in the hip-joints and in both legs. The pain was not entirely confined to his joints, at times he experienced a cramp-like pain in the calf muscles, which would "draw up into a knot." Shortly after the onset of these symptoms the patient's friends noted that he was limping. The patient himself had not been aware of this. One year before he consulted a physician, who told him that his right leg was bowed and that it was about three-quarters of an inch shorter than the left. To equalize this difference in the lengths of the two extremities the patient began to wear a higher heel on the right shoe. The patient considered the pain in the back worse than that in the legs;

it was of a dull, intermittent character, entirely absent during sleep, and in the waking hours it was worse when the patient stood than when he walked. His average height had been 5 ft. 10½ inches; his weight had varied between 170 and 180 pounds. He did not believe that his head had changed in size, for he had always worn a No. 7¼ hat with comfort.

Physical Examination. July 10, 1913. The patient was a well-nourished man of large frame and good stature; height, 5 feet 6 inches. There was well-marked alopecia capitis and pigmentation of the exposed parts; the mucous membranes were of excellent color. The patient looked unusually robust and normal in appearance.

Skeletal System. There was nothing, on general inspection, which would attract the observer's attention to the bony framework. The patient stood slightly inclined toward the right, which appeared to be due to the outward and anterior bowing of the right thigh; this explained also the downward tilting of the pelvis on the right side, and accounted for the limping gait.

The head appeared massive, but not out of proportion to the rest of the bony framework; the calvarium was prominent, but it was not enlarged in comparison with the features.

MEASUREMENTS OF THE HEAD.

	Cm.
Occipitofrontal circumference (maximum)	57.0
Occipitofrontal diameter	19.5
Occipitomenital diameter	21.5
Biparietal diameter.	15.5
Suboccipitobregmatic diameter	17.0
Suboccipitobregmatic circumference	54.5
Bitemporal diameter	15.0
Circumference of vault from meatus to meatus	38.0

Thorax. The thorax presented no special abnormalities; it was somewhat barrel-shaped; its circumference at the top of the axilla measured 95 cm.

Spine. There was no evidence of kyphosis or scoliosis at any level of the spine. On pressure over the spine in the cervical and dorsal regions no tenderness was elicited; in the lumbar region, however, the erector spinæ group of muscles were held spastic, obliterating the normal lumbar lordosis; pressure over this region caused pain. There was no pain directly over the sacro-iliac articulations. The range of motion of the spine was fairly good in all directions.

The bony pelvis was not broader or heavier than normal; the distance between the lower border of the ribs and the iliac crests was not decreased. Measurements of the pelvis showed the following: intereristal diameter, 29 cm.; interspinous diameter, 25 cm.; intertrochanteric diameter, 32.5 cm.

Upper Extremities. The arms did not appear disproportionately long. Both humeri were straight; no thickening or roughening could be made out on palpation. The radius and ulna on both sides were straight and showed no abnormalities. The grand expansion of the arms measured 171.25 cm. (68.5 inches).

Lower Extremities. The right lower extremity presented the special point of interest; the right thigh was markedly bowed anteriorly and laterally; the bowing was considerable, so that with the heels together the internal condyles of the femora were separated a distance of 4.5 cm. On palpation the right femur was found to be more massive, thicker, somewhat more nodular, and rougher through its whole length than its fellow. There was no tenderness elicited on deep pressure, and there was no evidence of any local inflammatory lesion. On extending the leg and flexing the thigh upon the abdomen, more pain was caused on the left side than on the right, due to a relaxation of the hamstring muscles beneath the bowed right femur.

MEASUREMENTS OF THE LOWER EXTREMITIES.

	Cm. right.	Cm. left.
Anterior superior spine to internal malleolus	86.0	88.5
Umbilicus to internal malleolus	98.5	100.0
Anterior superior spine to internal condyle of femur	47.0	49.5
Circumference of thigh 20 cm. above midpatellar region.	47.5	46.0
Circumference of calf 20 cm. below midpatellar region	30.5	30.5
Circumference of ankles above malleoli	19.5	19.5

From the measurements it was evident that the right leg was 2.5 cm. shorter than the left, and that the shortening of the whole leg, as measured from the anterior superior spine to the internal malleolus, equaled the shortening of the right femur as measured from the anterior superior spine to the internal condyle; therefore, the shortening of the right leg was due entirely to shortening of the right femur.

Both tibiae appeared straight; there was not the slightest anterior or lateral bowing. On palpation both bones felt normal.

General Examination. The temporal arteries were not tortuous. Eyes were not prominent; pupils reacted to light and on accommodation; extra-ocular movements were good. Teeth were slightly carious; there was extensive dental work. Pharynx was negative. There was no general glandular enlargement.

Lungs. Hyperresonant; clear on percussion and auscultation.

Heart. Cardiac dullness extended 12 cm. to the left and 4.5 cm. to the right of the midsternal line; heart sounds were clear. Pulse showed no abnormalities; blood-pressure, 140 (Tykos).

Abdomen. Normal to inspection. Liver dullness extended to the costal margin. Spleen was not palpable.

Reflexes. Present in both upper and lower extremities.

Wassermann reaction was negative in May, 1913.

Radiographic Examination (skiagram Nos. 18334 and 18965. Reported by Dr. F. H. Baetjer). *Skull*: Skull showed slight diffuse chronic thickening of inner and outer tables. Exostosis at occipital tuberosity. Sella normal in size and shape; solid sella. Calcification of pineal body. *Right femur* (Fig. 1): Femur showed well-marked bowing. Head of femur was bent, producing coxa vara. There was chronic diffuse thickening of entire shaft of femur; medullary canal could be easily made out and did not seem to be involved. Thickening through shaft of bone was uniform throughout, with some slight interlinear striations. Notwithstanding the fact that there were pieces of bullet scattered throughout the leg, the condition did not impress one as an osteomyelitis, but rather as Paget's disease. *Left femur*: Normal in every respect. *Right tibia and fibula*: Slight periostitis of tibia; fibula showed normal variation.

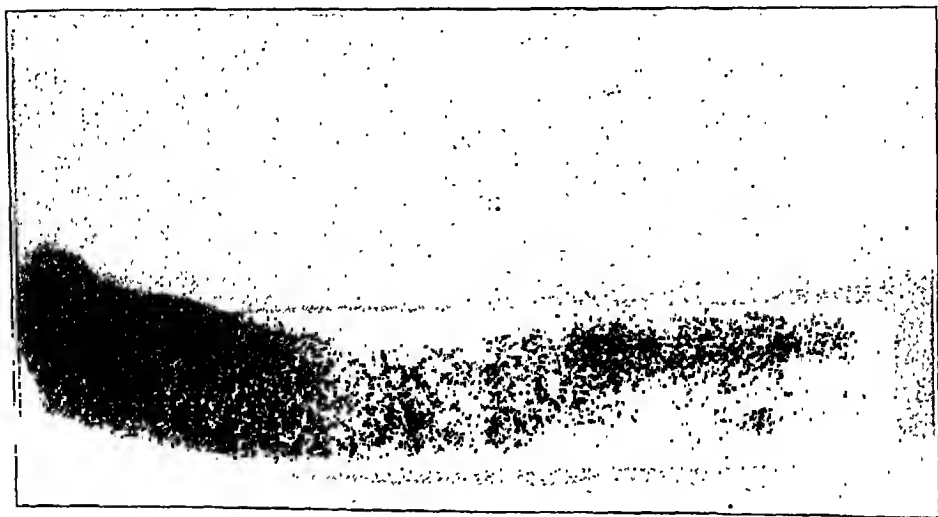


FIG. 1.—Skiagram of right femur, showing bowing and chronic diffuse thickening of entire shaft of the bone. (Thickening of shaft of bone is uniform throughout, with some slight interlinear striations). Medullary canal can be easily made out and does not seem to be involved.

Summary. There were certain points in the history and examination of this patient which deserve special mention: (1) the history of typhoid fever at the age of eighteen years, the possible history of lues, with the slight periostitis of the right tibia (Wassermann reaction negative), and the history of a gunshot wound in the right thigh fifteen or eighteen years before, must be kept in mind as a possible etiology for the deformity, although the subsequent history and radiographic study did not support this view; (2) the insidious onset, at the age of fifty-two years, of bowing and thickening of the right femur, and the characteristic association of this deformity with vague rheumatic pains; (3) the remarkable localization of the morbid process in one bone, although the disease had

lasted probably for a period of more than four years; (4) the presence in the skiagrams of the right femur, of the bony changes which characterized the disease, and their absence in other bones.

The name *ostitis deformans* was given by Czerný⁴ to a disease of bone described by him in 1873. The subject of this disease was a young soldier, aged twenty-two years, who subsequent to the exposure and fatigue of a military campaign began to suffer from continuous pains in the left leg, followed in several months by the spontaneous development of curvature in the tibia and fibula of this leg. Because of the sequence of the pathological changes observed in these bones—softening, bending, and hardening—Czerný was inclined to regard the condition as a chronic inflammation rather than as a localized form of osteomalacia.

Three years later, Sir James Paget⁵ used the term *osteitis deformans* for a well-defined and slowly progressive disease which now bears his name. Unlike the localized malady described by Czerný, the disease described by Paget is characterized clinically by an involvement of a large part of the skeleton. According to him the affection is usually symmetrical, and attacks most frequently the skull and the long bones of the lower extremities; the latter enlarge, soften, and become unnaturally curved and misshapen. It would appear, therefore, that, although clinically different, the same pathological process underlies the localized as well as the more generalized form of this obscure disease of bone.

Since the appearance of the communications by Czerný and by Paget a considerable number of cases characterized by bending and hardening of one or two long bones have been reported as instances of Paget's disease, although the exact relationship of these two disease types is still not clear. Some authors are of the opinion that "multiplicity of the bones affected is the constant characteristic"⁶ of the disease described by Paget. Schirmer,⁷ however, concludes from his collective study that there are true instances of *osteitis deformans* (Paget) in which for years the deformity remains limited to one bone, and in which it is difficult to predict whether or not the disease will progressively involve other parts of the skeleton. This view is also held by Schlesinger,⁸ who designates the localized as the "monoösteitic" form of *osteitis deformans*; whereas both Stegmann⁹ and Latzko¹⁰ maintain that the etiology of the morbid process which leads to the bending and thickening of a single bone is, in all probability, different from that of Paget's disease.

CASES OF OSTEITIS DEFORMANS (MONOÖSTEITIC FORM) RECORDED IN THE LITERATURE.—A critical analysis of the cases reported in

⁴ Wien. med. Woch., 1873, xxiii, 894.

⁵ Loc. cit.

⁶ Fitz, Trans. Assoc. Amer. Phys., 1902, xvii, 395 and 402.

⁷ Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1903, xi, 561, 609, 641, 689, 721.

⁸ Mitteilungen d. Ges. f. innere Med. u. Kinderheilk., Wien, 1907, vi, 61; *ibid.*, 1908, vii, 99.

⁹ Katholicky, Wien. klin. Woch., 1905, xviii, 619 and 649 (Discussion).

¹⁰ *Ibid.*

the literature as osteitis deformans (Paget) in which the disease remained limited to a single bone shows that a small number only properly belong to this group. Many of the others, as will appear later, are definitely instances of luetic osteitis, bone tumor, sarcoma, carcinoma or myeloma, and of spontaneous fractures, with bending and with thickening due to excessive callus formation.

Studies of the morbid anatomy of osteitis deformans (Paget) have led to the knowledge that this disease is associated with pathological changes in the bone which are, more or less, constant; in the main, the pathological findings of Paget¹¹ and Butlin have been confirmed by later investigators, von Recklinghausen,¹² Stilling,¹³ Packard, Steele and Kirkbride,¹⁴ and Higbee and Ellis.¹⁵ Moreover, studies of skiagrams of bones affected with Paget's disease have made it possible not only to recognize the gross pathological anatomical changes during life, but to differentiate them from other morbid processes affecting one or more long bones, especially those of syphilitic origin.¹⁶ It would be well, therefore, to accept at present as instances of Paget's disease only those cases which have been confirmed either by pathological or radiographic study.

Of this localized form of the affection there are probably not more than five or six cases recorded up to the year 1908, in which pathological or x-ray study has confirmed the clinical diagnosis. Bowlby,¹⁷ in 1883, described a case of osteitis deformans in which the right femur alone was involved. This case I should like to present in some detail, since a search of the literature shows that it is the only other instance of proved Paget's disease on record in which one femur alone was involved:

"C. G., aged sixty-four years, a cabman, was admitted to St. Bartholomew's Hospital on August 23, 1882, suffering from an injury to the head, which caused death fourteen days later. No measurements of the thighs were made during life, and the patient was not in a condition to give any history of his previous health; it was noticed, however, that the right femur was much curved in an outward and forward direction, and was shorter than its fellow. After death his son, who was an intelligent man, told me that his father's leg had gradually become curved during the last ten years of his life, that it had not caused him any pain, and that he had frequently measured both limbs, with the view of ascertaining the amount and progress of the shortening, which a few months before death amounted to two and a half inches. He had often suffered from gout, mostly in the great toe, but was otherwise healthy. A postmortem examination showed that the only bone affected was the femur of the left (?) side."¹⁸

¹¹ Loc. cit.

¹² Virchows Arch., 1890, exix, 542.

¹³ Jour. Med. Research, 1911, xix, 55.

¹⁷ Trans. Path. Soc. Lond., 1883, xxxiv, 192.

¹² Festschr. d. Assistenten f. Virchow, 1891.

¹⁴ Trans. Assoc. Amer. Phys., 1901, xvi, 666.

¹⁵ Zeitschr. f. Heill, 1902, xxiii, 130.

¹⁸ Ibid, 193.

The most striking features made out from a pathological study of this diseased bone are noted in the description of the photograph of the specimen reproduced from the *Illustrated Medical News* for February 23, 1889, which contains an abstract of this case (Fig. 2).

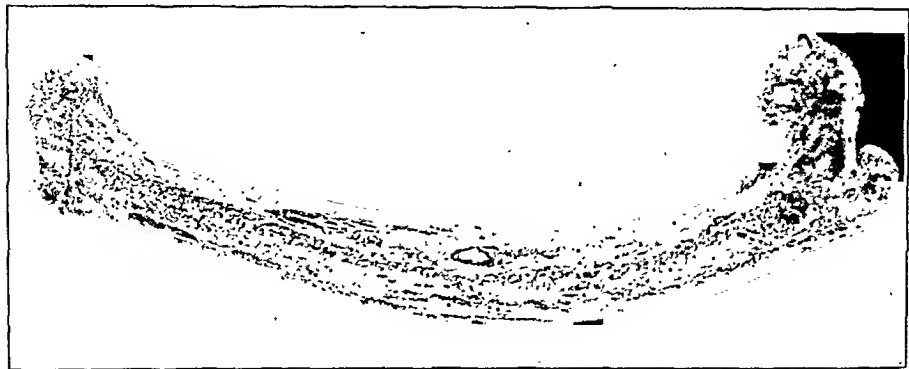


FIG. 2.—Osteitis deformans involving a single bone. (After Bowlby, *Illustrated Medical News*, 1889, ii, 188). Shows curvature of femur; shaft is increased in circumference. Neck of bone is placed at right angles to shaft. Medullary canal is irregular in shape; its caliber is encroached upon by new bone, partly of a hard porcellaneous appearance and partly of a cancellous nature.

A similar case, reported by Benno Schmidt¹⁹ about ten years earlier, has additional interest, since during the period of observation, four years, the disease subsided in the right femur, where it began, and involved the left tibia. The patient was an apothecary, aged fifty-six years; he gave no history of trauma, lues, or other infections. According to the patient's account he began to have pain in the right thigh, and later noticed that his right femur was beginning to bow. The right leg became 2 cm. shorter than its fellow. About four years after the onset of the malady the process subsided in the right femur only to begin in the left tibia. Unfortunately the diagnosis of this case was not verified by anatomical study. The record is of interest because it shows that this disease may remain localized in one bone for a number of years, only later to manifest itself in some other part of the skeleton, and that patients who are reported to have this affection in one bone may develop it later in its more generalized form.

More recently Schmieden²⁰ and Katholicky²¹ have reported a single case, and Schlesinger two cases of this "monoösteitic" form of osteitis deformans. In every one of these cases a characteristic feature was involvement of one tibia. The diagnosis was confirmed in each instance by histological or radiographic study.

Schmieden's patient was a woman, aged fifty-eight years, without a history or stigma of lues. At the age of fifty-two years, without

¹⁹ Arch. f. Heilk., 1874, xv, 81

²¹ Loc. cit.

²⁰ Deut. Zeitschr. f. Chir., 1903, lxx, 207.

apparent cause, she gradually developed thickening and bowing of the right tibia. No similar changes were demonstrable in any other bones of the body. Histological examination of material obtained, first by an osteotomy and later by amputation, showed the pathological features to which reference already has been made: disappearance of the normal bone, its replacement by osteoid tissue, with a destruction of the fatty marrow, and its conversion into connective tissue. In this particular case, skiagrams showed that the cortex had almost disappeared, and it was apparent from microscopic study that the process of bone absorption had progressed more rapidly than that of new bone formation.

Similarly, Katholicky's patient also was a woman, aged sixty years, who for ten years had observed that her tibia was gradually bending and thickening; the fibula remained normal and straight, and looked like a string to a bow represented by the bent tibia. It was demonstrated by x-ray examination that the entire lamellar architecture of the tibia was changed, and that there was evidence of decalcification and new bone formation.

Both of Schlesinger's²² patients were men, one aged sixty-two years, and the other sixty-four years; in both the right tibia was the only bone affected. The first patient was observed twelve years, and during this interval no other bone became diseased, not even the fibula of the same extremity. In both cases the typical changes of Paget's disease were present on x-ray examination.

Schlesinger is inclined to place all such instances of osteitis deformans, with involvement of a single bone, into a special group which he calls the "monoösteitic" form of Paget's disease. This form he characterizes as follows: "The disease begins insidiously without trauma (without a history of lues), may continue for years without attracting the patient's attention, and is usually discovered accidentally. In all of the author's three cases the changes were well advanced before the disease was discovered by the physician. Pain appears to be absent; in this respect it differs from the types described by Joncheray, of which the painless form affects only the upper extremities. The power of walking is not greatly interfered with, even though the deformity of the tibia (thickening and bending) is far advanced. This point has been emphasized by Paget also. The disease affects the tibia, and as it appears, especially in front. It does not progress in spite of years' duration and apparently involves no other bones."²³

Besides the cases mentioned, there are on record a number of examples which may belong to the "monoösteitic" form of Paget's disease. In most of these the clinical diagnosis has not been substantiated by anatomical or x-ray examination, and the clinical facts presented are so meager as to make one question whether

²² Loc cit.

²³ Mitteilungen d. Ges. f. innere Med. u. Kinderheilk, Wien, 1908, vii, 101.

they are really instances of this disease at all. To this doubtful group belong the cases which Czerny²⁴ collected from the literature: those of Seoutetten, Solly, Mosetig, and Weinlechner. The clinical descriptions of their patients are not convincing; besides all of them, with one exception, the second case of Solly, were not over thirty years of age at the time the disease began; whereas it is rare for osteitis deformans to begin before the fifth or sixth decades. Likewise the patient of Volkmann²⁵ was a boy, aged nineteen years, in whom the left tibia became bent spontaneously; Volkmann regarded this as an instance of chronic osteitis, but its identity with osteitis deformans (Paget) is doubtful.

In their dissertations on osteitis deformans both Patschu²⁶ and Gliner²⁷ cite a number of examples in which the disease affected one bone. In each instance the diagnosis was based upon unverified clinical observation; from these it is obvious that a large number of the cases mentioned belong to diseases other than osteitis deformans. The case of Isreal, for instance, which both authors classify under osteitis deformans, proved after amputation to be a fracture of the left femur, with dislocation of the fragments and excessive callus formation; again, the patients of Martini and of Küster were both suffering from pathological fractures of the femur at the site of tumors. So, too, the case of Wolff, cited at some length by Patschu, is another instance of pathological fracture rather than of osteitis deformans. It is evident, therefore, that numerous unrelated affections have been improperly classified as osteitis deformans.

DIFFERENTIAL DIAGNOSIS.—The generalized form of osteitis deformans (Paget) presents so characteristic a clinical picture that it is easily recognized; but the more localized form of the disease, especially when the affection remains limited to one bone for many years, presents difficulties for diagnosis because it may resemble very closely other affections of bone. Syphilitic disease of bone, osteitis fibrosa, and certain other diffuse new formations of bone may resemble the "monoosteitic" form of osteitis deformans.

Syphilitic disease of bone, like syphilitic disease of other tissues, may imitate other affections of bone so closely that it must always be borne in mind in any bone disease where the diagnosis is in doubt. Syphilitic periostitis with bone formation is a frequent lesion, especially in congenital lues. In this condition the tibia is most commonly involved; the bone is usually curved and shows a rarefying and condensing osteitis, with irregular periosteal and endosteal new bone formation. The condition may simulate so closely osteitis deformans that it has been designated osteitis deformans syphilitica.

²⁴ Loc. cit.

²⁵ Ueber deformierende Ostitis, Dissertation, Berlin, 1880.

²⁶ Ueber Ostitis deformans (Paget), Dissertation, Bern., 1910.

²⁷ Beitr. z. Chir., 1875, p. 148.

Few general rules are of value in so protean a disease as syphilis, but some of the following points may be of help to differentiate clinically the two conditions: (1) In acquired syphilis the bones of the cranium are more frequently involved than the long bones; in congenital syphilis, where the long bones, especially the tibiae, are most frequently the seat of the disease, the patients are young, whereas osteitis deformans (Paget) usually affects patients late in life; (2) in the syphilitic cases, in addition to the general enlargement, the affected bones often present irregular bosses on their surface; (3) in syphilitic disease, lesions, either of other bones or the soft tissues, are likely to be present at the same time; in congenital syphilis other obvious signs of the disease may exist; (4) the presence of osteoscopic pains is an important feature of syphilitic disease of bone; the pain is worse at night, is usually continuous, and has a boring character. In osteitis deformans the pain presents no constant characteristics; (5) in most cases of syphilis of bone the effect of treatment is usually pronounced; improvement under treatment to be of diagnostic value, however, must be marked and sustained; (6) careful study of the skiagrams of syphilitic bone affections and of osteitis deformans has shown that the two diseases can be differentiated radiographically.

Ostitis fibrosa (v. Recklinghausen's disease of bone; tumorbildenden ostitis deformans) is essentially an osteomalacia deformans which may involve the entire skeleton or appear in isolated portions; in the latter location it may be mistaken for osteitis deformans of the type under consideration.

Pathologically ostitis fibrosa and osteitis deformans are closely related, and some authors contend that the two diseases cannot be differentiated histologically. V. Recklinghausen, however, considers the disease described by him a separate entity, and emphasizes certain points of difference: in ostitis fibrosa there are regressive changes of the fibrous marrow into gelatinous cysts, and progressive changes leading to the formation in the long bones of small, brown, red tumors of the nature of giant-celled sarcomas; in osteitis deformans the bones are usually more curved and histological, and x-ray studies show that in this disease the changes in the bone marrow are less marked and the process of new bone formation more striking than in the type described by v. Recklinghausen. The two affections are unlike in another important respect, which is useful in the differentiation of these two conditions clinically: the occurrence of spontaneous fractures is almost pathognomonic of ostitis fibrosa, and according to Brunn,²⁸ it is one of the earliest indications of the existence of this malady; in osteitis deformans, on the contrary, spontaneous fractures are rare. Among 86 cases collected from the literature by Schirmer²⁹

²⁸ Beitr. z. klin. Chir., i, 72.

²⁹ Loc. cit., p. 646.

in 1908 there were only five instances of osteitis deformans associated with spontaneous fractures.

Of other forms of diffuse hyperostosis which may be limited to one bone and produce a clinical picture like localized osteitis deformans, two only deserve brief mention. One form is seen around osteomyelitic cavities, where, owing to a diffuse thickening of the spongy bone in association with a necrosis of the marrow cavities, hard new bone is formed; the process may involve also the compact bone and lead to considerable thickening of the shaft of the bone over a greater or less area. This condition can usually be differentiated from osteitis deformans by the history and the clinical symptoms given by the patient and by x -ray examination.

Another form of diffuse hyperostosis results from the complete ossification of an exuberant callus such as sometimes occurs after a fracture. Where this process is limited to a single bone it is readily differentiated from the "monoösteitic" form of osteitis deformans by the history and x -ray examination.

Although Paget's disease has been called by Katholicky and by Schmieden osteomalacia chronica deformans hypertrophica, clinically this affection and osteomalacia or halisteresis have little resemblance. Pathologically they may have this in common: in both diseases decalcification and softening of bone occur; in osteomalacia the process stops at this point, whereas in osteitis deformans decalcification is associated with new bone formation.

VALVULAR HEART DISEASE CONSIDERED AS A CONTRIBUTORY ETIOLOGICAL FACTOR IN PULMONARY TUBERCULOSIS: A COMPLICATION OF THE FIRST MAGNITUDE.

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In the clinic at North Reading I have taken particular interest in deriving a careful history relating to general and occupational habits of such cases of pulmonary tuberculosis as have exhibited definite signs of valvular heart disease. For from the matter of these histories it has appeared oftentimes quite suggestive that the cardiac disease has handicapped the patient's resistance to such an extent as to permit implantation and progress of tubercular disease.

In addition, I have kept clearly in mind the identity of each patient affected with this important complication, in order that I might modify or supplement in these cases the instructions laid down

for the care and treatment of tubercular patients. The resulting success in handling the patients in this manner and in directing their after-care has demonstrated at least to my mind a superiority of method which would not be obtained by regarding the cardiac irregularity only in a minor light.

In the first place, the supposition that valvular heart disease may predispose an individual to pulmonary tuberculosis is the antithesis of the accepted view established in the early part of the last century, and more or less adhered to down to the present time.

In 1844 Rokitansky's¹ almost classic assertion was made that those diseases of the heart and bloodvessels producing cyanosis were not compatible with tuberculosis, the cyanosis causing an "exquisite immunity." Again, the same author² made the statement convincingly that there was "the greatest practical importance in the fact that mechanical obstacles in the centre of the circulating system, or rather the heart producing increased 'venosity' in the lungs with resulting cyanosis, proceeded to act against tubercle." Pottenger³ believed Rokitansky's observations on the coincidence of heart disease and tuberculosis have been generally confirmed by modern observers, and explained the relative infrequency of dual occurrence to the fact that the hyperemia taking place in the lung in some forms of heart disease, caused therein a concentration of the blood with its protective bodies. The Bier method⁴ of treatment of tubercular parts by hyperemia was established through discovery that stenosis of the pulmonary artery, inducing anemia of the lung, was followed by pulmonary tuberculosis in a large percentage of cases, and, conversely, that hyperemia apparently had an immunizing power against tuberculosis of the lungs.

R. C. Cabot⁵ states that about one-quarter to one-third of all cases of pulmonary stenosis are complicated with pulmonary tuberculosis. However, he makes no mention of any antagonism of other forms of morbus cordis against pulmonary tuberculosis, nor does he venture an opinion as to the real factor in the causation of pulmonary tuberculosis in pulmonary stenosis cases, whether it may be anemia of the lung or the subnormal resistance of cardiac cases in general and pulmonary stenosis cases in particular. In this last respect, Babcock⁶ mentions that the congenital forms of pulmonary stenosis render the individuals weakly, undersized, and sometimes mentally deficient, and that they manifest a striking cyanosis. Therefore, we should expect them to be quite promising subjects for the growth and progress of tuberculosis.

Lawrason Brown⁷ speaks of the deviation of opinion upon this

¹ Handbuch der path. Anat., 1844, Band II, S. 520.

² Pulmonary Tuberculosis, 1908, p. 211.

³ Physical Diagnosis, 4th ed. p. 252.

⁴ Diseases of the Heart and Arterial System, p. 380.

⁵ AMER. JOUR. MED. SCI., 1909, cxxxvii, p. 186.

⁶ Ibid., 1846, Band I, S. 427.

⁷ Pottenger, loc. cit.

subject, and quotes Vierordt, who maintained that whatever frequency of occurrence there was of pulmonary tuberculosis in pulmonary stenosis cases was due to the lack of vitality and resistance common to any individual suffering from any congenital heart disease. Johanne Otto⁸ has stated that the simultaneous occurrence of the two lesions, that is, cardiac and pulmonary, is by no means incompatible, and, as a matter of fact, is rather ordinary in women especially, on account of lowered vitality due to the heart disease. She further averred that malnutrition of the cardiac muscle and insufficient compensatory hypertrophy, seen often in women, are conditions which render a tubercular infection more readily possible.

Hermann Vierordt⁹ took exception to Rokitansky's views, particularly concerning pulmonary stenosis as a cardiac lesion, and said that patients suffering from this variety of organic heart disease were predisposed to pulmonary tuberculosis.

Norris¹⁰ quite completely covers the ground relating to the concurrence of heart disease and pulmonary tuberculosis in an excellent dissertation in which he supported Vierordt's belief that the frequent occurrence of pulmonary tuberculosis was not limited to pulmonary stenosis alone, but is noted also in other varieties of congenital heart disease. He, however, did not believe pulmonary tuberculosis any more frequent in pulmonary stenosis or atresia than in the case of other conditions in which nutrition is profoundly impaired. Babcock believes that anything which like valvular disease impairs nutrition must necessarily lessen the likelihood of successful resistance to tuberculosis, and that when the combination of the two does occur it enhances the gravity of the prognosis, for they cannot fail to react injuriously on each other.

Osler¹¹ speaks of "a temporary disturbance of compensation" as a possible occurrence in heart disease when the loss of reserve force exists for a short and limited time and does not go on to complete decompensation. This interval seems attractive when considering the opportunity for implantation of pulmonary tuberculosis in an individual, for we might reasonably expect that at just such time when he is overcome by fatigue that he is all the more susceptible to infection. Since, as Osler says, reserve power of the normal heart can be affected abnormally by any interference with the cardiac muscle, such as infection, intoxication, and malnutrition, there must be a considerably larger adverse effect in the case of a morbid heart with its lessened reserve capacity and greater irritability. Poorly nourished, as many pretubercular individuals are, and with less strength to spare, it seems rightly conceiv-

⁸ Das Ausschliessungs verhältniss zwischen Herzklappenfehlern und Lungenschwindsucht, Virchows Archiv, 1896. Bd. cxliv.

⁹ Specielle Pathologie und Therapie, H. Nothnagel, XV. Band, II. "Die angeborenen Herzkrankheiten," p. 97. (Pulmonalstenose und Tuberculose.)

¹⁰ Tuberculosis and Heart Disease, AMER. JOUR. MED. SCI., October, 1904, p. 655.

¹¹ Modern Medicine, vol. iv, p. 210.

able that certain cardiac patients should be oppressed with the united conditions of subnormal resistance and overfatigue, the latter an invitation to infection and the former a frank admission of insufficient protection. Therefore, Sir William Collins' quotation has its significance: "The germ has, perhaps, been too much with us, and the paramount importance of soil has been absurdly underrated."¹²

There seems to be considerable variation among the published statistics concerning the incidence of pulmonary tuberculosis and valvular heart disease. At one extreme we have Kryger's¹³ figures in 1100 autopsies on tubercular subjects, in which only 10, or 0.9 per cent., showed cardiac disease, while in 59 autopsies on valvular disease cases all had healed or arrested tuberculosis.

Norris¹⁴ collected figures from the literature covering 8154 autopsies on tubercular subjects where 3.5 per cent. showed signs of valvular heart disease. He relates that the coincidence of valvular disease and pulmonary tuberculosis is encountered with only moderate infrequency, but that this condition has been more often recorded by recent than by old observers. He further reported 130 cases (7.3 per cent.) of valvular disease in 1764 autopsies which he himself performed on tubercular subjects.

Anders¹⁵ noted a 1.2 per cent. incidence in 10,687 cases at autopsy. L. Brown¹⁶ noted a figure as low as 0.9 per cent. valvular heart disease in a grand total of 71,115 cases of records collected abroad.

Carrington¹⁷ has reported 21 per cent. heart disease cases occurring in another series of cases of tuberculosis.

An autopsy report of the Phipps Institute¹⁸ noted organic disease of the heart and lungs as occurring coincidentally in 10.3 per cent. of 143 cases. Mitral were found to preponderate over aortic lesions. Comment was made upon the frequency with which the two conditions occurred together and the conclusion drawn that the tendency of clinical records is rather to underestimate than to overestimate this frequency.

In a later report¹⁹ from the same institution five cases of incompetency of the heart valves were found (6.7 per cent. in the 74 autopsies performed that year. The mitral valve was affected four times and the aortic twice. A summary for three years stated 21 valvular incompetencies or 0.6 per cent. in the 197 cases autopsied.

Shultz²⁰ found antecedent cardiac disease 42 times in 109 cases

¹² Draper's Research Memoirs. Karl Pearson, Studies in National Deterioration, 11.

¹³ Ueber das gleichzeitige Vorkommen von Lungentuberculose und Klappenfehler des linken Herzens, Münchener Dissertation.

¹⁴ Loc. cit.

¹⁶ Brown loc. cit.

¹⁵ AMER. JOUR. MED. SCI., 1909, cxxiii, p. 93.

¹⁷ Cited by Norris, loc. cit.

¹⁸ Phipps Institute, Second Annual Report, 1904-1905.

¹⁹ Phipps Institute, Fifth Annual Report.

²⁰ Cited by Norris, loc. cit.

of tuberculosis, while similar instances might be quoted almost indefinitely.

L. Brown²¹ believed that the difficulty in reconciling the great differences among these figures was explained by the indifference with which tuberculosis has been treated at many general hospitals and the reluctance of some pathologists for performing autopsies in apparently uncomplicated cases of tuberculosis. Therefore, he thought the occurrence of the larger percentages of heart disease found by some pathologists might be readily explained. In my own experience many instances have come to light of patients admitted to the North Reading State Sanatorium with frank and long-standing heart disease complicated with pulmonary tuberculosis; and yet their application commitment papers made out and signed by their physician recorded no mention of their heart disease, the heart repeatedly being noted as "negative." In 46 cases where this complication existed the writer found only 6 wherein any mention of heart disease was made by the committing physician. These papers were selected at random from the 1400 application forms filed in our central office. Eighteen "negative," "heart normal," or "O.K." notations were found in the spaces reserved for heart examination records although they related to patients with frank valvular heart disease.

Accordingly, we are not always impressed by gross statistics regarding the coincidence of valvular heart disease and pulmonary tuberculosis, and we are less reluctant to state the results of our investigation at North Reading, although these, as compared with some of the low figures found in the literature, would appear rather startling.

In reviewing 1300 consecutive case records of patients admitted to and treated at the North Reading State Sanatorium in the past three years, my interest was aroused in this particular subject by the rather frequent occurrence of record of heart murmurs detected by the various members of the medical staff. To be sure, not all such adventitious sounds indicated organic disease of the heart, as many were attributed "functional," "cardiorespiratory," or "undetermined."

However, without further mention of the undetermined murmurs, we found definite records of valvular heart disease in 228, or 17.53 per cent. of the 1300 case reports examined. Of the 605 female cases, 128, or 21.15 per cent. had cardiac disease, and of the 695 male cases, 100, or 14.3 per cent. were similarly complicated; of the former 74, or 57.8 per cent. were diagnosed as mitral regurgitation, 42 or 33.5 per cent. as mitral regurgitation and stenosis, and 12, or 9.3 per cent. as aortic regurgitation, 3 of the latter having also aortic stenosis, and 2 others of the 12 having mitral regurgitation with aortic regurgitation.

²¹ Loc. cit.

Of the men, 65 had mitral regurgitation, and of these 65 there were 28 showing also mitral stenosis. Aortic regurgitation appeared in 24 records, and together with aortic stenosis in 6 cases. 5 cases were recorded as "undertermined" in character, although noted as "valvular heart disease." Two of these were suggestive of tricuspid insufficiency according to the record, but no definite diagnosis as such was made.

It should be stated that approximately 75 per cent. of all cases admitted to the North Reading State Sanatorium have been in the third stage at time of admission. Some question, therefore, might be raised as to whether the valvular trouble was actually the primary disease. On this point L. Brown²² believed that very rarely did endocarditis occur in pulmonary tuberculosis, and that still more rarely was it a case where the tubercle bacillus was the infecting organism.

When heart disease of the inflammatory valvular type did develop during the course of pulmonary tuberculosis it was most often a late complication. He states that he has never seen such a case in the 3000 patients treated in his clinic.

Norris²³ in 11,655 autopsy records of tubercular subjects found recent endocarditis in 151 cases, or 1.3 per cent. Marshall²⁴ thought that acute endocarditis was present in 5 per cent. of all cases of tuberculosis. Brown²⁵ produced experimental tuberculosis in 6 dogs, inoculating them intravenously and treating them by zomotherapy, whereupon endocarditis occurred 4 times and hemorrhagic pericarditis once. However, this same author concludes that tubercular endocarditis is very rare. The writer has not had the experience of observing such a case at North Reading. A single instance he recalls of having suspected as developing a valvular lesion at the mitral orifice a short while previous to death, but in carefully reviewing this patient's history with the help of relatives, he came to the conclusion that there was undoubtedly some cardiac defect previous to the recognized onset of his tubercular trouble.

Tessier²⁶ has maintained that 40 per cent. of advanced cases of pulmonary tuberculosis develop atresia or stenosis of the mitral orifice, due to the action of the toxin in the circulating blood. However, this view is not heartily supported by other investigators, and Norris is quite skeptical as to Tessier's explanation of this phenomenon. As a matter of fact, the etiology of many of the valvular lesions was all in doubt, and but few gave any history of rheumatism or chorea or any other serious indisposition to which might be accorded the origin of the endocardial trouble. Nearly all the aortic insufficiency cases occurred in elderly people affected with arteriosclerosis.

²² Loc. cit.

²⁴ John Hopkins Hosp. Bull. 1905, xvi, p. 303.

²⁵ AMER. JOUR. MED. SCI., 1903, cxxv, 1071.

²³ Loc. cit.

²⁶ Cited by Norris.

Of far greater interest to me than the differential diagnosis of the various valvular lesions were the life histories leading up to the onset of lung trouble in the cardiac patients. Many instances were found of long hours worked out in poorly ventilated and dusty shops, together with a low grade state of nutrition. Some patients, especially young women, evidently had not partaken of a really substantial meal for days, and yet, suffering from overfatigue, had worked on at a gruelling occupation until tuberculosis had added the one insurmountable handicap to their endurance. The all-sufficient disadvantage of a disordered heart robbed them of whatever reserve strength they might normally have possessed.

In order to obtain greater abundance of detail on this very subject, and to carry out the investigation more to my own satisfaction, we took in hand the thorough examination of all pulmonary patients residing at one time in the Sanatorium, seeking to find those afflicted beyond all question of doubt with the complication of valvular heart disease. Then we went into the matter of their histories, comparing their lives with those of uncomplicated cases of tuberculosis, and learned that while the latter class had pursued similarly hard occupations and were as subject to deprivation or dissipation, or both, the cardiac patients were more certainly impressed with the conditions undermining their health. That is, things of little moment to the others were of major importance to these individuals whose labor was taken always at the cost of heart fatigue and irritability. A patient with normal heart but with bilateral lung disease thought almost nothing of his former ability to work from sunrise to sunset in a damp, ill-ventilated shop, but, on the other hand, the man with antecedent heart disease often attributed his lung trouble to "overwork" and lack of nourishment. Accentuation of the many obstacles in a laboring life, together with domestic responsibilities, was apparently felt by the latter case, who perhaps would have escaped phthisical disease had his heart been sound.

Among the 183 patients examined, we found 29 cases of frank valvular heart disease; of the 183 there were 98 males and 85 females, and of the former 15 were affected and of the latter 14. That is, 15.3 per cent. of the males and 16.47 per cent. of the females examined, presented cardiac lesions. Two of these individuals, one male and one female, have not as yet been determined tubercular. Inoculations of their sputa in a series of guinea-pigs have repeatedly produced negative results, and the conclusion is now suggested that they are suffering mainly from heart disease rather than pulmonary tuberculosis. In the case of the woman slight hemorrhages are occurring from time to time, and there is pronounced mitral regurgitation, with imperfect compensatory hypertrophy of the heart muscle, but there are no definite signs in the lungs such as might indicate a tubercular process.

With the man, forty years of age, a history of syphilis with confirmatory signs and symptoms seems to account for his aortic regurgitation with a fairly well-developed compensation. No evidence of tuberculosis can at present be found in his lungs.

Therefore, it would be better to state 27 cases of pulmonary tuberculosis complicated with valvular heart disease, that is 14.75 per cent. Among the men, excluding the one probably non-tubercular case mentioned above, there were 13 cases of mitral insufficiency, including 5 cases of mitral stenosis combined with regurgitation, and 1 case of aortic regurgitation. The last case appeared in an elderly man who presented marked arteriosclerosis, which undoubtedly was the cause of his aortic insufficiency; compensation was practically nil, and he died of pulmonary tuberculosis shortly after admission.

Of the women, excluding the non-tubercular case, each of the 13 exhibited mitral regurgitation, including 2 who also had mitral stenosis.

The average age of the men affected is thirty-one years and of the women twenty-nine years, which diverges very little from the figures representing the average respective ages of all the men and all the women admitted at the Sanatorium during the hospital year 1911 to 1912. In investigating the etiological factors in the causation of their morbid conditions in this series of cases we had the advantage of "live" histories; by which is meant that the patients were present to answer whatever questions were desired regarding their former occupations and habits, whereas the information available in past histories was often lacking in certain interesting detail.

Accordingly, opportunity was offered in comparing the living regimen of our cardiac class with that of the uncomplicated. The failure of certain patients with long-standing heart disease to select proper occupations which would be more in accordance with their cardiac infirmities, and to favor their weakness in that direction, seems the cause of their succumbing to tuberculosis. It is not that they worked harder, or perhaps even so arduously as did others with sound heart, but, as a matter of fact, it is apparent that they were not competing on an even basis with normal man. The hardships of a grinding occupation were relatively greater to our cardiac patient, and in the same way, deprivation and dissipation were relatively more effective against him. Hence, his one means of escape from pulmonary tuberculosis would have been in seeking a selective occupation, and at the same time maintaining even and well-regulated habits.

The majority of the cardiac class were never told of their morbid heart condition, although they were ready to admit that they had for a long time realized something wrong with that organ. Dyspnea, especially ascending a flight of stairs, palpitation, and extraordinary

fatigue in the later hours of the day are common symptoms complained of, indicating oftentimes that the cardiac affection had existed long before the onset of tubercular disease.

One patient, a woman aged twenty-four years, worked in printing establishments for eight years previous to the discovery that her lungs were affected. While following this occupation she tried to maintain a nine- to ten-hour daily schedule in poorly ventilated dusty shops, breathing vitiated air and occasionally developing such cyanosis as to excite comment from her fellow employees. Her meals were hasty affairs, and of minimum quantity. Afternoon weariness was extreme, the patient stating that "she was ready to drop" at the closing hour; on arriving home at 7 P.M. she would be too tired to eat supper, which was the only really substantial meal provided for the day. There is sharp demarcation between the sluggish progress of her mitral disease and the sudden onset of pulmonary tuberculosis, so that it must be evident that she was not suffering all that time from incipient tuberculosis. That the soil was gradually prepared for pulmonary disease by the slowly grinding down action of an overburdened heart seems feasible.

Two young men gave nearly identical occupational histories. They were brass workers, and in their work were subjected to breathing fine metallic dust and impure air, but, as a matter of fact, could not recall a single case of consumption as having occurred among the employees of their respective shops, although all were under the same conditions. Each patient, upon examination, presented frank mitral disease as well as advanced consumption, with bilateral lung involvement. Each had noticed for several years that he became short of breath upon moderate exertion sooner than other men, and particularly that when excited his heart would beat very fast and "pound in his ears." A matter of interest was, however, their realization of becoming tired more easily than other fellow-employees and of their wornout condition as they finished their day's work.

Another pulmonary and heart case was seen in a man who for a number of years had followed the express-delivery business necessitating much running up and down stairs and heavy lifting. An excessive alcoholic habit had its inimical influence upon this man, and no doubt had as much to do in bringing on his tubercular trouble as had his strenuous occupation. However, here again was seen the sudden onset of tuberculosis which appeared as a new, clearly defined symptom-complex, superimposed on the minor manifestations of his heart trouble.

Thus did many histories of the cardiac class fall in the same category, of which those mentioned in the foregoing are fair examples. Overexertion in their daily occupations, overindulgence in excesses of a vicious nature, and lowered nutrition are the factors

conducting a lowered resistance in patients with valvular heart disease, and hence inviting tubercular infection.

Babcock²⁷ writes: "All authors are agreed in the declaration that nothing in the daily life of cardiac patients affects their hearts and the prognosis more disastrously than does severe and prolonged or too oft-repeated physical exertion. The day laborer who earns his daily bread by the sweat of the brow cannot be expected to keep his compensation intact for so long as will he whose vocation does not subject his heart to the possibility of overstrain."

A semiconclusion is herein suggested: namely, that individuals with valvular heart disease should know and appreciate the significance of their infirmity in order that they may choose occupations well adapted for their condition. In this manner a smaller number of such patients would contract pulmonary tuberculosis. Systematic physical examinations of factory employes by reliable clinicians must be the easier way of solving this problem, thus eliminating the pretubercular from the certainty of future infection.

Dr. Herman Vickery, of the Massachusetts General Hospital, said as he addressed a group of medical students gathered at the bedside of a cardiac patient, occupation an iceman, admitted to the hospital with disordered compensation: "Every heart case should have a certificate affirming his crippled condition, and with a notice to the public that this man, although to all outward appearances physically sound and strong, is handicapped by a serious infirmity."

With regard to the care and treatment of tuberculosis complicated with valvular heart disease we believe that we must strive and hope for not only the arrest of the tubercular process, but also the restoration of full compensation of the heart. The heart's irritability, accentuated by the toxemia of tuberculosis, is very striking in active cases, and not until we have secured a placid condition in that organ may we hope for any improvement in the pulmonary foci of disturbance. Accordingly, I find it well to encourage my complicated case to especially avoid excitement, and to take a maximum amount of rest at proper intervals. Worry and insomnia are most prominent, and must be considered seriously by the physician who should attempt to eliminate the former by suggestive thought and pleasant distraction of the patient's mind.

We heartily agree with Babcock's²⁸ affirmation that no other class of cases so amply rewards intelligent and painstaking management as cardiac patients. This idea seems to apply as well to those complicated with tuberculosis, although, of course, there are more obstacles to overcome.

Medicinal treatment does not appeal at all strongly to us for this line of cases, excepting the use of digitalis and strychnine

²⁷ Loc. cit., p. 409.

²⁸ Loc. cit., p. 477.

as indicated. Depletive purgation is an effective remedy when hemorrhage occurs.

Diet is important and disordered digestion must be met with rest and proper non-irritating nourishment, rather than medication.

Intelligently prescribed exercise has a very important place with this class of pulmonary patients, and should be regarded as a strong adjunct in treating the convalescent case. Only in the individual case can any advice be given on this matter; hence the uselessness of laying down any general instructions.

Finally, we wish to emphasize the need of treating the patient with every consideration which is consistent with the maintenance of firm discipline over his daily life at the sanatorium, and with the carefully guarded security of his respect for and confidence in his medical adviser.

SOME OBSERVATIONS ON THE CLASSIFICATION AND TREATMENT OF HEMOPTYSIS.

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WHILE papers dealing with hemoptysis appear at frequent intervals in medical literature, yet we are far from having a clear understanding of this complication from either the standpoint of its causation or treatment.

While all blood which comes from the lungs in sufficient quantities to show distinct color may be regarded as hemoptysis, yet there are different factors which cause the blood to escape from the vessels. Inasmuch as the condition which causes the escape of the blood should be taken into consideration in determining our mode of treating the hemoptysis, it is desirable to form some idea of the pathological condition which is present in and surrounding the areas from which the bleeding comes.

My study of hemoptysis is based largely on my sanatorium experience. My patients for the most part have been those well advanced in the disease. The first observation which I wish to emphasize is the fact that hemoptyses come in groups. They come at the time when the barometer is rapidly changing. At such times we nearly always have not a single one but several patients reported as "spitting blood." In our experience we have noted that foggy weather, rainy weather, as well as changes to extremely dry are all accompanied by this complication. The great majority of hemoptyses, as we find them, are slight, amounting to less than a half-ounce, although we occasionally meet quite large ones; not as large, as a rule, however, as the patients and attendants think.

According to my observation hemoptysis may be divided into the following classes:

1. A frank hemorrhage where a vessel of some size is opened and the blood flows out freely. The blood comes up into the mouth as fast as the patient can expectorate it, and in severe cases faster; occasionally causing immediate death of the patient. The blood in these cases is nearly always a bright red. The cause of this type of bleeding is the erosion of a vessel or the rupture of an aneurysm. The amount of bleeding depends on the size of the vessel involved and the extent of the rupture in its wall. This type of bleeding usually comes on suddenly, without warning, and without any previous change in symptoms. Occasionally, however, traces of blood have shown in the sputum during the day or days previous. It is the most serious of all types, and requires the greatest care in treatment.

2. A bleeding which comes on coincident with the expulsion of a necrotic mass. This type is usually preceded by several days' rise of temperature and the symptoms which accompany the increased absorption of toxins. The real cause of the bleeding in these cases is that the destructive process goes on rapidly and the wall of the abscess breaks before the vessels have been obliterated by the inflammatory process. This type of bleeding usually comes from small vessels which close quickly. At least, in my experience, it has rarely proved serious. The amount of blood lost is usually small, rarely more than a few mouthfuls at a time. This type is distinctly different from the preceding one in the way it is brought on, yet it calls for much the same treatment. Following this type of hemorrhage the patient is usually better, at least temporarily; not because of the hemorrhage, however, but because the expulsion of the tuberculous mass has given him relief.

3. A type when there is no distinct quantity of blood, but the mucus raised is mixed with color giving it a characteristic dull, pinkish color. This I consider as coming from the small vessels in the wall of a cavity. I usually consider this a sign of stimulation in the cavity, and take it to be a condition favorable to healing. This form of hemoptysis is not serious, and requires no special treatment.

4. The type of hemoptysis where the patient keeps expectorating mouthfuls of blood for several days, sometimes for weeks. There is never very much at a time, rarely more than a few mouthfuls, but this may be repeated day after day. The blood may be bright red, especially when the quantity is a half-ounce or more; or, what is more common, it is somewhat dark in appearance. I look upon this type as being due to a congestion, much the same as we see in pneumonia and heart lesions. Is it not possible, however, that it might be due to toxic action? The difficulty in this type is to recognize it. We cannot be sure of our diagnosis. This type calls

for distinctly different treatment from the types where vessels are open, but it takes a considerable amount of boldness to go against our conservative traditions. This type does not prove fatal, but serious damage seems to occur when it continues for a long time, whether the hemorrhage itself has any part in the deleterious result, or whether it is due wholly to the condition which produces it, is open to some question.

When we consider the various drugs which have been used in the treatment of hemorrhage, and take into account their supposed action on the pulmonary circulation, we must either conclude that their action is practically *nil* or that nature is able to overcome any harm that might be done by them, for the patient usually survives.

In types 1 and 2 there is a vessel open which nature closes with a clot, and there is a tendency for bleeding to continue until the opening is firmly closed. It is imperative to retain the clot in the opening until it has organized and sealed the vessel. To this end everything must be done that will quiet the circulatory system. Both mental and physical rest should be insisted upon. The mental rest can oftentimes be obtained through reassuring the patient and giving him confidence and hope. Where this cannot be done, a hypodermic injection of morphine is to be resorted to. Personally, I do not like to use morphine when I can avoid it, yet at the same time it meets two important indications in the treatment of hemorrhage: (1) it quiets the patient, and (2) it reduces the tendency to cough. When I do resort to morphine I rarely give a large dose, but usually employ $\frac{1}{16}$ grain hypodermically. This small dose seems to have a decidedly sedative action and avoids the severer blunting effect on the nerve endings of the respiratory tract, which follows larger doses. I feel that great harm is often done in the treatment of hemorrhage by large and repeated doses of morphine. It prevents the patient clearing out the blood from the respiratory tract, and thus favors a complicating pneumonia.

For the maintenance of physical rest the patient should be put to bed in a comfortable position, usually on his back, with shoulders a little high; and, if the bleeding has been severe, no movement should be allowed. During the first twenty-four hours, as a rule, he becomes tired of the position, but after that he lies with comparatively little discomfort. He should be kept quiet until all danger of recurrence has disappeared. After there has been no further bleeding for twenty-four hours, the nurse should change his position by rolling him over on his side and holding him there with a pillow. He should not be allowed to sit up in bed until all color has disappeared from the sputum for at least three days. Of course, where the hemorrhage is slight such stringent regulations are not necessary, but in a severe hemorrhage, these measures are often life-saving.

In way of medication, as a rule, reliance should be placed upon

tincture of *veratrum viridi*, giving five drops every three hours until the pulse slows, then reducing the dose to four drops or three drops every four or five hours. The *veratrum* is somewhat slow in its action, and in order to get an immediate effect, we use nitroglycerin, $\frac{1}{100}$ to $\frac{1}{50}$ grain, dissolved on the patient's tongue. A hypodermic tablet of nitroglycerine dissolved on the tongue will produce an effect in a few minutes, and then by the time its action is passing off the *veratrum* is beginning to show its effect.

Recently we have been trying pituitrin in some of these cases. It seems to promise well as far as we have observed it. It has been shown to raise systemic blood-pressure and lower that of the pulmonary circulation. In several patients treated with it the bleeding seemed to stop more promptly than is usually the case. Another action which we noticed in 2 cases was an evacuation of the bowels within a few moments after the remedy was absorbed. We have employed it in doses of $\frac{1}{2}$ to 1 c.c., repeated in four hours.

Artificial pneumothorax is often valuable in types 1 and 2.

For that type of hemoptysis which we have designated as "congestive," mentioned as type 4, we would use a different line of treatment. It is difficult at first to be sure that a hemoptysis belongs to this type; in fact, it is necessary to study a case for a few days, as a rule, before this can be determined definitely; and we think it is safest to treat every case at first as though it were an open vessel. If it is of the congestive or toxic type, it is apt to be prolonged, the spitting of blood will continue for quite a little time, not in large quantities but small quantities each day, and numerous times during the day. We keep the patient, suffering from this type, quiet, just the same as those suffering from the other types, but instead of using *veratrum* and nitroglycerin, we use some circulatory stimulant. These are the cases that we think obtain decided benefit from the adrenal preparations. *Digitalis* also works well at times and we also feel that *strychnine* is sometimes of decided benefit.

There are numerous complications associated with hemorrhage which require some attention. They are not well understood, and are not always easy to handle. We often see a marked shock following a hemorrhage, even although the amount of blood lost is small; and there are times when it seems that respiratory failure is threatened. Under such conditions we have felt in one or two instances that the life was probably saved by the use of *strychnine*. Two complications that are not uncommon in hemorrhage are paralysis or paresis of the bladder and of the bowel. Obstinate constipation follows a hemorrhage in many instances, and the strange thing is that ordinary cathartics in these cases fail to act. In several severe hemorrhages we have seen it necessary to remove the feces from the bowel mechanically. After experimenting a great deal with various laxatives in these cases we have found that the rhubarb pill seems to act the best of all remedies. In these cases

we give 5 grains of rhubarb, three or four times a day, and in most instances it seems to act well. We have also seen a few cases where it was necessary to catheterize the patient following hemorrhage.

The question has often been discussed as to the harm or benefit arising from hemorrhage. We do not believe that hemorrhage, *per se*, ever does the patient any good, although we have seen numerous instances where the patient improved following the hemorrhage. This was not on account of the hemorrhage, however, but because of the fact that the hemorrhage was due to the rupture and expulsion of a necrotic mass, as a result of which the patient was relieved of toxic symptoms. The second type of hemorrhage mentioned is often followed by an improvement in the condition of the patient. The following case illustrates this point:

T. W., aged forty-eight years, suffering from active process in the lung. Was running high temperature, as high as 103°, with severe intoxication, mental and physical depression, night sweats, and severe prostration. An abscess formed in the lung. His sputum increased markedly, and the increase was accompanied by a hemorrhage. The temperature dropped considerably and gave the patient relief. A few days later the abscess opened freely and a large quantity of pus was poured out, giving complete relief from temperature and toxemia. The hemorrhage did not cause the amelioration of symptoms, but the rupture of the abscess did.

Hemorrhage may be harmful in several ways. Following the opening of a vessel, bacilli may escape into the blood-stream and cause a dissemination of the disease. We have seen several instances where an acute disseminated tuberculosis followed hemorrhage.

Another common complication which often proves harmful is an accompanying pneumonia. From the blood which trickles down into the lung an irritation is set up and pneumonia results, which, in some instances, leaves considerable damage after it has finally subsided.

A CASE OF CONGENITAL ABSENCE OF THE LOWER HALF OF THE INTERAURICULAR SEPTUM.

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MALFORMATIONS of the septa of the heart, while not common, are not unique. There are, in all probability, many more cases of potentially patent foramen ovale than are ever diagnosed or even suspected, owing to the absence of symptoms, which autopsy readily explains in showing the defect to be due to the non-union of overlapping edges of the foramen which the pressure of the blood keeps

tightly in apposition, the foramen thereby being functionally, if not anatomically, closed.

The case herewith reported derives its particular interest, not alone from the extent of the defect, but more from the complete absence of any symptoms referable to the condition which was found at autopsy.

Theoretically, a lesion so extensive and of so functionally important a character should have given rise to grave and significant symptoms, and markedly affected both the health and the general development of the individual; in spite of the fact, however, that the case was under treatment essentially for cardiac defects and that particular care was, therefore, directed toward the heart and all symptoms referable to it, no suspicion of the existing abnormality was aroused in any way.

The clinical history was as follows:

Florence A., aged eighteen years, was admitted to the University Hospital on January 25, 1913, for dyspnea, palpitation, and pain in the right knee. The history, taken shortly after admission, was as follows:

History of Present Illness. So far as she can remember the patient has always been prone to dyspnea and palpitation on moderate exertion, but never, until the present attack, to such a degree as to arouse her apprehension or specifically direct her attention to it.

About January 1, 1913, she began to have severe headaches, accompanied by constant backache, dyspnea, and palpitation, these latter being so pronounced at times as to preclude sleep. There is no history of precordial pain during these attacks.

January 24 she had severe, sharp pains in her right knee, but does not know whether it also became red or swollen. She was admitted to the hospital the following day, and within the next few days, in the order cited, the pain spread to her right foot, right hand, right elbow, and right shoulder, the parts becoming red and swollen, as well as painful; within the next week her left foot and left knee were attacked in the same manner.

Her dyspnea, she thinks, has not become noticeably increased, but she is conscious at times of a rather marked palpitation. She has never at any time had any swelling of the feet other than that just mentioned, nor has there ever been any puffiness of the face.

She complains that, occasionally, and especially since she has been in the hospital, she sweats at night, but gives no history of previous night sweats nor constant cough. Since admission she has had a slight, spasmodic cough, which she attributes to "throat irritation," and which is accompanied by some slight morning expectoration of whitish mucus.

Her appetite, until recently, has always been good and her bowels regular. At times she has had attacks of "indigestion," accompanied

by gaseous distention to such a degree that she is unable to wear corsets, but these attacks seem to be associated with dietetic errors, and questioning fails to elicit anything which would point to the abdominal distention being in any way ascitic in character.

She gives no history of other disorders other than the menstrual history given below.

Past Medical History. Measles, parotitis, varicella, and scarlatina in childhood; later influenza and frequent attacks of tonsillitis. No history of chorea, pneumonia, typhoid fever, nor rheumatism other than the present attack.

Until she was nine years of age she was a somnambulist; always had vivid dreams, and talked in her sleep, the two latter conditions being still present to a somewhat lessened degree. Beyond the attacks of "indigestion," cited above, there is no history of gastrointestinal disturbance.

Menstrual History. The menses began when thirteen years of age, when she was confined to her bed for three weeks before their appearance. They have always been painful for the first two or three days, and the flow, when established, lasts, as a rule, for five or six days. She is irregular, often missing for a time, the last period not appearing until twelve weeks after the preceding one, lasting for a week, and then after the intermission of a week, again appearing for another week.

She contracts colds easily in the winter, but says they are not of long duration.

While always, she says, "inclined to be delicate," she gives no history of specific complaint, and says she was in her usual condition of health until January, 1912, when, while on a visit to Wyoming, she contracted an attack of "la grippe," which confined her to bed for two weeks, at times with a temperature of 106°, and from which she did not sufficiently convalesce to be able to travel until one month after its inception.

From the following February until June she felt about as well as usual; by this she means that she was conscious of no subjective symptoms other than moderate dyspnea on exertion, and then only to what she considered a normal degree, and had no specific complaints; but in June she began to feel languid and tired, lost her appetite, and was attacked with severe frontal, occipital, and parietal headaches, together with dyspnea and palpitation, sufficiently marked to lead her to consult a physician, who told her that she had "cardiac trouble."

Under treatment she improved perceptibly, the palpitation and dyspnea becoming negligible, and she was not particularly ill, although consulting her doctor once or twice a month, until the day after Thanksgiving, when she again had a slight attack of what she called "la grippe," which kept her in bed for two days. On her recovery from this illness she felt languid, tired, and without

energy until Christmas, when, for a short time, she felt better. Shortly after this date, however, her dyspnea again began to become troublesome, and she developed acute inflammation in her knee, and from this point on the story is taken up in the history of her present illness.

Family History. Negative.

Physical Examination. The patient is a rather slender, pale, and delicate-looking white girl of nervous, high-strung appearance, giving no external evidence of pain nor marked dyspnea.

The skin is fair and clear, the eyes bright, and the cheeks flushed, due, in part, to dilatation of the finer capillaries, which are plainly seen through the skin; fine, bluish veins are also seen over the temples and in the neck. Of small frame, the general nutrition is fair, and there is no evidence of recent emaciation.

The general appearance is that of a young girl underdeveloped physically and younger looking than her age, of a rather infantile type in appearance:

There are no gross abnormalities of the head or face.

There is some slight play of the alæ with respiration, more so than is accounted for by the degree of dyspnea present at this time.

The lips are dry, slightly scaly, and pale. The eyes are bright, with equal pupils reacting normally to light, convergence, and accommodation; the sclera are clear.

The neck is rather slender, and the superficial veins are clearly seen through the skin, and on each side there is a marked systolic pulsation in the larger vessels.

The throat is negative; the mucous membranes are much paler than normal; the tongue is coated with a brownish fur, approaching closely to the edges; the teeth are well formed and in good condition, though there is a slight degree of pyorrhea, and the gums are also paler than normal.

The hands are small and slender, with a slight tendency toward broadening at the ends of the fingers, and a slight cyanosis of the nail-beds. The right hand is swathed in bandages and gauze, and the fingers, when exposed, are very slightly swollen, slightly reddened, hot to the touch, but not markedly tender nor painful except on semiflexion.

There are no masses nor roughenings over the tendons, no bone tenderness, and no apparent joint effusions of marked degree. There are no glandular enlargements in either the elbow or axilla.

Both knees and feet are wrapped in gauze and bandages; there is, however, no limitation of motion nor tenderness on handling; the affected parts are not conspicuously red nor swollen, and there is no edema over the tibia.

Thorax. The skin is fair and clear, moist, and warm, with no marked eruptions nor gross abnormalities. The superficial veins are easily seen, though not markedly dilated.

The chest is well-formed and of fair development, and although the patient is not of muscular nor adipose build, there is no apparent evidence of loss of weight; the ribs, however, while not prominent, are clearly outlined beneath the flesh.

There are no gross abnormalities of the bony frame-work suggestive of rickets or other like condition.

The breasts are of moderate size and normal in shape, but slightly underdeveloped, with large nipples but no apparent areola.

Expansion is fair and equal on both sides. The accessory muscles of respiration are not markedly active, and there are no marked supraclavicular or infraclavicular depressions. There is an evident systolic pulsation in the costal angle, and, in the region of the apex, a diffuse, heaving impulse is plainly visible.

Lungs. Anteriorly the percussion note is normal, with the exception of a suggestion of hyperresonance at the apices; there are no areas of dulness. Both tactile fremitus and vocal resonance seem slightly increased at the apices, and down to about the fourth rib. The breath sounds are rapid, slightly harsh, and inspiration is loud. There are no rales. Posteriorly the percussion note is normal, but tactile fremitus and vocal resonance are slightly increased throughout. The breath-sounds are slightly harsh, and tend somewhat toward a tubular character at the bases; inspiration is prolonged, and on the left side about the angle of the scapula a few creaking rales are heard, but not constantly.

Heart. Upper border, third rib; right base, 5 cm.; left base, 11.5 cm.; right oblique, 9.5 cm.; left oblique, 14.5 cm.; height, 8.5 cm.

On admission the apex-beat was diffuse, and was quite close to the midaxillary line; there was a marked gallop rhythm, and the heart was so rapid that it was difficult to time the murmurs, of which there were several present: a harsh, presystolic murmur at the apex, merging into the first sound, and a suggestion of a diastolic murmur at the aortic area. The pulmonic first sound was harsh and murmurish, the pulmonic second much accentuated and slapping.

Later, when the heart had quieted somewhat, a more thorough examination was possible and revealed the following conditions:

At this examination, four days after admission, the apex beat was situated 3 cm. outside the nipple line, and presented a somewhat heaving, diffuse impulse; there was also a suggestion of a thrill at this area.

The heart measurements at this time were as follows:

Upper border, third rib; right base, 2.3 cm.; left base, 11 cm.; right oblique, 13 cm.; left oblique, 14 cm.

At the mitral area there is a double murmur: a somewhat harsh, systolic murmur, long and blowing, and a soft, purring, diastolic murmur. The sounds are slappy and forcible.

The murmurs, especially the systolic, are transmitted into the

axilla, and are well heard as far out as the axillary line; here they become somewhat fainter and begin to diminish in intensity, while the heart sounds become more clear, until, at the angle of the left scapula, the murmurs are lost while the heart sounds are well heard, both forcible and slappy, the second sound markedly accented.

Over the tricuspid area the same murmurs are heard, although not so loudly, and the sounds are transmitted for a short distance up the sternum. It is not clear at this examination whether the sounds heard at the tricuspid area are transmitted from the mitral area or whether there is, in addition, a tricuspid lesion; the latter seems slightly more probable.

Over the aorta there is a distinct systolic thrill, and, on auscultation, a harsh, systolic murmur and a blowing diastolic murmur, which are transmitted upward into the vessels of the neck, loud over the carotids, fainter in the vessels of the neck itself.

The pulmonic second sound is strongly accented, but auscultation of this area reveals no other abnormalities.

Abdomen. The abdomen is of normal shape, size, and conformation, and presents no gross evidences of swellings nor tumor masses. There are no eruptions, the skin is clear, and there are no marked engorgements of the superficial veins.

The abdominal wall is relaxed and the skin is warm and moist. There is an evident epigastric pulsation.

The stomach does not appear to be markedly distended nor ptosed so far as can be ascertained through percussion; peristalsis is active, and there appears to be a moderate amount of gas present.

The liver extends from the sixth rib to 5 cm. below the costal margin, and on percussion is slightly tender. The spleen and kidneys are not palpable.

The inguinal glands are not enlarged, and there are no herniæ present.

No pelvic masses nor tenderness can be demonstrated.

Temperature, 99°; pulse, 100; respirations, 36.

Blood. Hemoglobin, 70 per cent.; red-blood cells, 3,680,000; white-blood cells, 16,400; polymorphonuclear, 72 per cent.; lymphocytes, 27 per cent.; large mononuclears, 1 per cent.

Urine. Amount, 500 c.c.; color: dark amber, cloudy, nebular sediment; specific gravity, 1.030; reaction, acid; albumin, light cloud (ferrocyanide test); sugar, none; sediment: no casts, cylindroids, nor red-blood cells; a little mucus, a few leukocytes and epithelial cells; no crystals.

Blood-pressure: Systolic, 94 mm.; diastolic, 62 mm.

Such was the condition of the patient when first seen by me, and on the above findings a diagnosis was made of acute, infectious arthritis complicated by an acute exacerbation of a chronic endocarditis, and treatment was instituted accordingly.

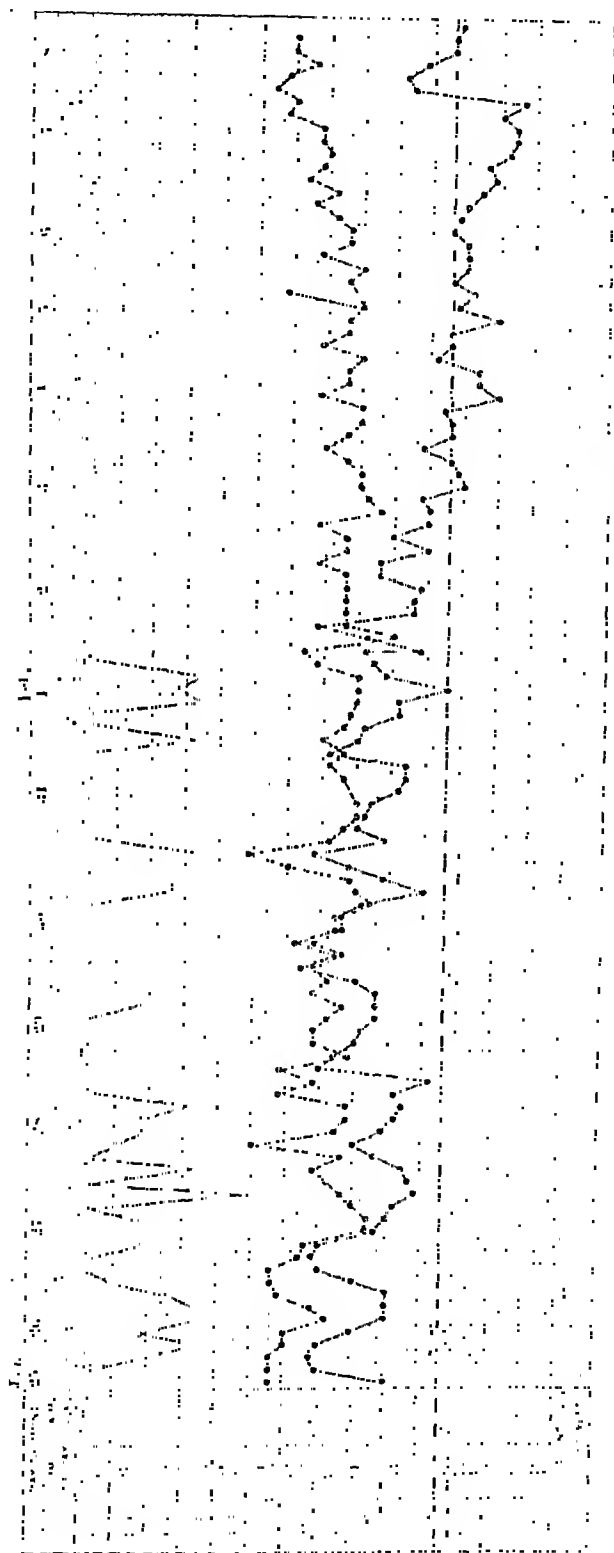


Fig. 1.—Clinical chart: 0—0 = respirations. •—•—• = pulse rate. •—•—• = temperature.

A double mitral insufficiency, due to a preceding endocarditis, was readily diagnosed on the history and character and constancy of the findings in this area, as was also an aortic stenosis. The tricuspid murmurs, however, were for some time the subject of discussion, so confusing were the shifting murmurs, due to the acute process, and the transmission of those due to the mitral lesion; eventually a tentative diagnosis of a more moderate grade of tricuspid stenosis was adopted.

The course of the disease was, at first, uneventful and presented about the usual condition of affairs to be expected of such a condition, as may be seen from the attached temperature chart and clinical record. Three days after admission some skodaic resonance and bronchophony were noted over the left base posteriorly, and six days after admission a capillary pulse was observed. The size of the liver was subject to some fluctuation, though never reaching normal, and at no time was the temperature very high. It is of great interest to note that at no time until the end, despite the high respiration rate which was a feature of the case and significant of the marked cardiac embarrassment, was there any cyanosis of sufficient moment to be noted on the daily records.

Shortly, however, an increasing leukocytosis became a marked feature of the blood examination, the count rising as high as 24,400; the dyspnea began to increase, the patient became toxic, restless, and distressed, especially at night, and a drop of temperature with a rapid pulse became a noticeable feature of the night records. In reference to this latter feature, it may be remarked that this was probably an incorrect record; the temperature was taken by mouth and the low levels were in all probability largely due to marked dyspnea and the consequent passage of large amounts of air over the bulb of the thermometer.

On the thirteenth day after admission there was a decided change in the condition, the following note being recorded:

"On entering the ward today the patient is lying on her right side, evidently dyspneic, the movements of the chest, alæ of the nose, and accessory muscles of respiration being distinct, and is evidently not as well as yesterday.

"When turned on her back she complains, becomes perceptibly uncomfortable, and pronouncedly more dyspneic than before, the respirations going to fifty-six per minute.

"She is restless, says she does not feel good, and complains of 'hot flashes,' and that she did not sleep well. The chart records a steady fall of temperature during the night, to 96.8, from which this morning there has been no recovery. The respiration rate is 54, and the pulse 124 per minute.

"Her position and condition attracted attention to her lungs, and, on examination, there was found a marked dulness of the upper right lobe, while over the entire left lung, both anteriorly

and posteriorly, the note is about normal. In the right upper lobe anteriorly and throughout there are many rales, and the breath-sounds are bronchial in type; there are comparatively few rales in the left lung, mainly at the base, and the breath sounds are not so decidedly bronchial.

"Diagnosis is made of lobar pneumonia of the right upper lobe.

"The pulse is rapid, and there is a gallop rhythm at the apex, the apical impulse being diffuse and heaving. The mitral murmur is fainter today; the sounds at the aortic area remain about the same as yesterday (no murmur at that time, but the sounds are very slappy and accentuated)."

In spite of attempts to stimulate the heart and improve the general condition, there was no marked improvement, and the subsequent course of the case was as follows:

Later in the same afternoon the patient became markedly cyanotic and dyspneic, the heart extremely irregular in action, and the general condition poor. She was bled sixteen ounces from the arm, and oxygen was administered, with decided improvement, which, however, as after-events showed, was only temporary. At this time her temperature by mouth was 96° and by rectum 99.2° . A similar attack occurred later in the evening, which was relieved to some extent by the administration of oxygen, heart stimulants, venesection, and saline infusion; but from midnight on her condition grew steadily worse, and she became more and more cyanotic, with marked palpitation, cardiac irregularity, and dyspnea, and death occurred at 8 A.M. the following morning.

Permission was obtained for a limited autopsy, the express condition being that all of the tissues and organs be replaced.

The autopsy, which was performed by Dr. K. M. Lynch, of the pathological department, is briefly abstracted below:

Autopsy 4081-13-6, F. A., Body of a young white woman, well formed and well preserved; about 5 feet four inches in height. Rigor mortis slight; livor mortis fairly well marked over dependent portions of the body. Skin white and dry; mammary glands fairly well developed. External surface of the body in good condition.

Abdominal cavity contains about 200 to 300 c.c. of clear fluid.

Membrane smooth and glistening. The liver extends about three fingers' breadths below the costal margin across the midline. Mesenteric lymph nodes enlarged, hard, and calcified; probably tuberculous.

Spleen: Small, firm, cuts with increased resistance, and on section is of a dark, blue-red, slaty color, and shows slaty induration and a chronic passive congestion.

Kidneys: Right weighs 140 grams, the left 130 grams. Capsule slightly adherent; on section shows cyanotic induration; ureters patulous.

Liver: The liver weighs 140 grams, and is slightly enlarged for

the size of the individual. The organ is flabby, cuts with leathery firmness, surfaces smooth and capsule transparent, and on section shows a mottled red and white appearance, the white areas being areas of degeneration and the red areas of congestion; vessels all enlarged and contain dark red blood; there is a rough, granular, retracted condition of the cut surface, which is decidedly firm. The organ shows parenchymatous degeneration, passive congestion, and early cirrhosis of the cardiac type.

The above is a brief extract of the more prominent gross findings in the more important abdominal organs, the features of most interest being noted in the chest, the examination of which follows in full:

Thorax: On opening the breastplate the whole anterior portion of the chest is apparently filled with the heart. It extends from about the upper border of the sternum downward on the right to the junction of the cartilage and the bone, over to the left with a blunt apex outside the nipple line, and almost to the axillary line at the sixth rib. The pleural cavities are both free from fluid or adhesions; both lungs are collapsed somewhat in the posterior portion of the cavities; membranes smooth and glistening.

Pericardium: The pericardium shows a smooth, glistening membrane, and contains several excessive centimeters of clear, straw-colored fluid. As the heart lies, the whole anterior surface is formed by the right heart. The pulmonary artery is much enlarged, the aorta very small.

Heart: The organ is some three or four times the size of the normal heart for this sized individual. It is of somewhat rounded, blunt-pointed shape; the majority is formed of the right side of the heart. The surface is smooth, and there is very little subpericardial tissue.

Incision into the different cavities reveals but little fluid blood, the right side of the heart being filled with a large mass of firm chicken-fat clot, while the left side contains a small amount of chicken fat and quite a large currant-jelly clot. The lowest portion of both ventricles contains a decidedly black-colored clot of the muratic variety.

The organ, when emptied, weighs 570 grams. It is decidedly flabby, the myocardium being rather pale, with decreased consistence. The right ventricular wall measures an average of 1 mm. in width, the right auricular wall an average of from 2 to 7 mm. in width. The papillary muscles of both cavities show an enormous increase in size.

The wall of the left ventricle averages 9 mm. in width, the left auricle from 1 to 4 mm. in width. The walls of these cavities are decidedly firmer and redder than on the right, and the papillary muscles show no distinct increase in size. The cavities of both auricles and of the right ventricle are decidedly enlarged; that of the left ventricle but little enlarged.

The mitral valve leaflets are decidedly thickened, retracted and adherent to each other at the ends. The orifice measures 2.5 cm. in its long diameter, and when split, 1.5 cm. in width. The valve leaflets are unusually abundant with large thick chordæ tendineæ extending even up to the base of the leaflets.

The aortic orifice measures 4.5 cm. in circumference, and is extremely small, hardly admitting the index finger; the valve leaflets are in good condition and the aorta enlarged somewhat beyond the aortic ring, but is never as large as it should be. Its intima is smooth and glistening, and the wall is elastic.

The tricuspid orifice measures 13.5 cm. in circumference. The leaflets are about the normal length, thin and translucent. The pulmonary artery throughout its entire length is decidedly much too large.

The wall, however, is about normal in appearance, elastic, and with a smooth, yellowish-white intima.

At the line of closure on the auricular side of the mitral valve leaflets there is a decided line of yellowish-white or reddish-white, small, fibrinous vegetations.

Both auricles, or rather what should be both auricles, are very much dilated, especially the right, which is also distinctly hypertrophied. The papillary muscles are larger than those ordinarily seen on the wall of the left ventricle.

These two cavities are merely separated from each other by a thin, semilunar flap of endocardial tissue extending from the roof in a half-moon shape down into the cavity, thus leaving an opening between the two auricles, measuring, without stretching at all, 3 cm. in diameter, which is well rounded; on the floor of the cavity, formed by the two auricles, there is no septum whatever.

The mitral orifices naturally come close together, and the bases of their valves are only separated by a matter of 2 to 3 cm.

In the thin, semilunar partition between the two auricles and the roof are two smaller openings, one about 2 mm. in diameter, and one about 4 mm. in diameter, the larger one being about the position and about the shape and size of a patulous foramen ovale. It has a flap of endocardial tissue coming down over it like a functionally closed foramen ovale. There are no evidences of inflammatory trouble around either of these openings, and all are apparently congenital.

The figure following is a diagrammatic representation of the conditions found in the heart, representing these as seen in a sagittal section of the organ.

The discovery of such an extensive cardiac lesion was an entirely unsuspected factor in the case, and in view of the entire absence

of any indication of congenital abnormality, aroused great interest and opened up a wide field of speculation in search of some explanation of the apparent functional compensation which had taken place.

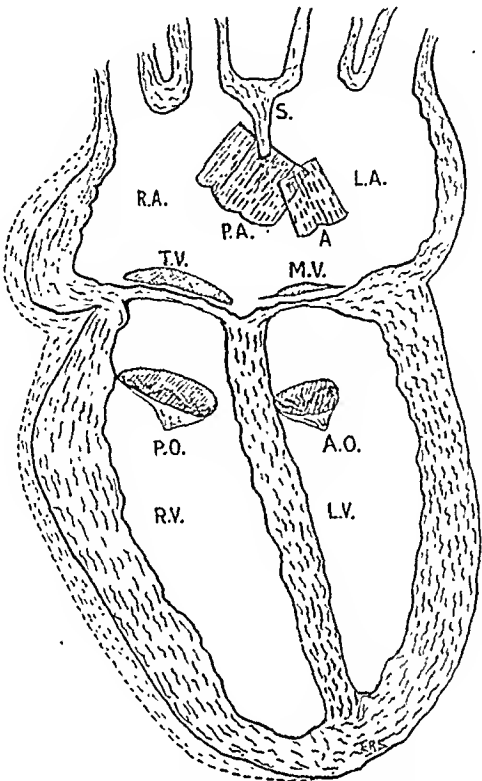


Fig. 2.—Diagrammatic drawing of conditions found in the heart.

Weight	570 gms.	Normal.
Right ventricular wall diameter	1 cm.	250 grams.
Right auricular wall diameter.	2-7 mm.	4 mm.
Left ventricular wall diameter	9 mm.	2 mm.
Left auricular wall diameter	2-4 mm.	9 mm.
Mitral orifice	2.5 cm. long.	2 mm.
	1.5 cm. wide.	circumference: 9 cm.
Aortic orifice	4.5 cm. circumference.	8 cm.
Tricuspid orifice	13.5 cm. circumference.	11 cm.
Pulmonary orifice	10.0 cm. circumference.	7 cm.
R. A.	Right auricle.	P. A. Pulmonary artery.
L. A.	Left auricle.	A. Aorta.
R. V.	Right ventricle.	T. V. Tricuspid valve.
L. V.	Left ventricle.	M. V. Mitral valve.
S.	Septum.	A. O. Aortic orifice.
P. O.	Pulmonary orifice.	

The question first presenting itself was, naturally, whether or not the condition was congenital or had been acquired in late life, and this leads to a brief review of the development of the heart insofar as we are enabled to elaborate it from a study of comparative anatomy.

Starting as a result of the fusion of the two primitive vessels, with a simple tube, fairly straight and of fairly uniform caliber, changes in form and in the relative position of its various parts soon take place. It soon becomes irregularly enlarged and a series of four dilatations with intervening constrictions are distinguishable; these dilatations, from behind forward, are (a) the sinus venosus, (b) the auricle, (c) the ventricle, and (d) the bulbus arteriosus. The short constriction between the auricle and the ventricle is known as the auricular canal. Meanwhile an elongation and bending of the tube takes place, resulting in the formation of a U-shaped loop, the posterior or venous end lying to the left and above. Subsequently the auricle ascends behind the ventricle.

While these changes have been taking place, the division of the heart cavity into its permanent chambers commences, the separation of the auricles being the point of particular interest in connection with this case. This occurs through the growth of a septum and through the thickening and fusion of the middle portion of the auricular canal, these thickenings being termed the endocardial cushions. The separation of the primitive auricle into right and left portions is indicated by the appearance of a groove on the upper and posterior wall, opposite which an auricular septum grows downward into the interior of the auricle. Its lower border gradually approaches the endocardial cushion in the auricular canal, and, for a time, a small opening is left between the upper end of the endocardial cushion and the lower end of the septum. This is the ostium primum, which later is closed by the fusion of the cushion with the septum, but before its closure is completed, an aperture appears in the upper part of the septum; this latter aperture, the ostium secundum, becomes the foramen ovale. A second auricular septum, the septum secundum, grows downward to the right of the first; its lower margin grows downward past the foramen ovale, but stops some distance from the posterior wall of the auricle, and, after birth, through fusion with the first, closes the foramen.

Applying these facts to the case at hand, we note, first of all, the absence of any sign of inflammatory trouble either in the flap-like partition itself or in the openings in its wall; further, the destruction and absorption of such a large amount of tissue as would be necessary to produce a like condition is manifestly improbable, if not incompatible, with existence; certainly, it could not have occurred without the signs of a grave illness, any mention of which is not found in the medical history of the patient.

Were it not for the opening so closely resembling in size and position, as well as in appearance, the foramen ovale as seen in the normal interauricular septum, the thought would occur that the condition was due to an absence of the interauricular septum as a whole and its representation by the persistence of the normally transitory septum spurium which, in the embryo, grows downward

from the roof of the auricle and is continuous with the right and left halves of the sinus venosus. The presence of the foramen ovale, however, or what closely resembles it, normally closed off by an overlying endocardial flap, forces the conclusion that the condition was due to a cessation of development and growth downward of the two interauricular septa which never reached, and consequently never fused, with the endocardial cushions. How to explain this lack of growth, affecting both septa, is, of course, a matter for purely hypothetical speculation, and, while it is recognized that a fetal endocarditis may occur and is not an uncommon cause of congenital septal defects, indications of such a condition are not demonstrable in this case and do not appear probable.

Of more interest is the explanation, if possible, of the functional compensation which apparently took place in this individual.

The comparatively normal growth and development of the patient is evidence, *per se*, that the cardiac defect occasioned no trouble during her intra-uterine existence; this is readily explainable when the peculiarities of the fetal circulation are recalled.

Normally, in the fetus, the blood entering the right auricle, is guided by the Eustachian valve through the foramen ovale into the left auricle where it becomes mixed with a small amount of blood returned from the lungs by the pulmonary veins; from the left auricle it passes into the left ventricle and thence to the aorta to gain the systemic circulation. In this individual the absence of the interauricular septum merely replaced the normal fetal condition in allowing a free communication between the auricles. At birth, however, a marked change takes place and the conditions in this case became at once extremely abnormal.

Normally, when respiration is established, an increased amount of blood from the pulmonary artery passes through the lungs which now perform their office as respiratory organs. Almost immediately after birth the foramen ovale is closed by the apposition of the valvular edge of the septum secundum against the annulus ovalis, the continued contact being due to respiration which increases the pressure in the left auricle, fusion and closure normally occurring about the tenth day after birth.

In this individual, however, no such condition obtained, and there remained, anatomically, a large area of wide and free communication between the auricles permitting, and, indeed, necessitating, an intimate mixture of venous and arterial blood.

The immediate result of such a condition is cyanosis and of an extreme grade, and it may be remarked, in passing, that in no class of ambulatory cases is cyanosis so pronounced and extreme as in those of congenital heart disease. The familiar "blue baby" is a striking example of the effects of a relatively moderate mixture of venous and arterial blood, an example with the picture and the results of which everyone is familiar; here, however, was an indi-

vidual in whom there should have been practically an absolute mixture of the two streams, and who, notwithstanding, was not a "blue baby," was never cyanosed, was never, until almost sixteen years after her birth, conscious of any cardiac abnormality of function, who exhibited no outward sign of failing or weakened circulation, who presented no clubbing of the fingers or toes, who evidenced no sign of marked physical or mental lack of development, who led a normal though probably quiet life, who contracted, in addition, valvular lesions, adding to the embarrassment of the heart, and who, nevertheless, died at the age of eighteen from an intercurrent infection with her congenital malformation entirely unsuspected.

How is this to be explained? The conclusion is almost unavoidable that functionally the defect did not exist, that it was in some manner entirely compensated. The assumption is born out by several facts which are noted in the examination of the heart itself.

In the first place there was a marked hypertrophy of the wall of what should have been the right auricle, while the wall of the left auricle was not correspondingly developed. Unless these two cavities were, during life, separated from one another to some extent, and capable of acting as separate compartments, hypertrophy of the wall of one could not very well occur without hypertrophy of the wall of the other. Again, the fact that the foramen ovale, or what apparently represented it in the remnant of the interauricular septum, was normally closed by the fusion of the overlying, valve-like flap of endocardial tissue is evidence that more or less pressure was exerted on these two surfaces to keep them in apposition; normally this is due to the higher pressure in the left auricle due to respiration, and, since fusion occurred in this case, there was probably such an increased pressure in the left auricle which must, therefore, have acted as a separate chamber. Thirdly, and what is most striking because it is fact and not speculative, there is the absence of any symptoms of imperfect oxygenation of the arterial stream which must have occurred unless, by some manner, the right auricular chamber was shut off—at least to a great extent—from the left. It seems justifiable, therefore, in fact, almost unavoidable, to assume that such a separation into independent chambers acting independently did take place; the possible mechanism by which it might have occurred will be noted later, when it will be seen that, while accounting for the hypertrophy to some extent, and for the closure of the foramen, it cannot, however, be adduced as the main or only factor in the functional compensation.

The case, as a whole, presents many interesting features, but perhaps the most striking is the entire absence of cyanosis, even a slight degree of which, as the patient was a pronounced blonde, with a fair and clear complexion, would have been at once evident.

There are several theories on which this might be explained: First, on the supposition that the two auricles were functionally, if not anatomically, separated, and that contamination of the arterial with the venous blood occurred only to a slight degree; the mechanism of such an occurrence, however, and exactly how it could have occurred in the presence of such conditions as were found so as to prevent the mixture of the two streams, we are unable to conceive or explain. The closing off of the two chambers is conceivable by some such mechanism as the following: with each contraction of the auricles the fringe representing the septum necessarily approached to a lesser or greater degree the floor of the auricles. Assuming a contraction of sufficient force, we could imagine the approximation of the fringe and the auricular floor, thus shutting off the two chambers and making of them functionally separate cavities. This, however, does not satisfactorily explain the lack of cyanosis, because such an approximation would necessarily have to occur when the auricles were emptying themselves of blood; immediately following there occurs auricular diastole, when the blood flows in from the *venæ cavæ* and the pulmonary veins into the two chambers, and the auricles are relaxed. If they are relaxed the septum would not be completed and the mixture of blood would, therefore, take place, the separation into separate compartments taking place in auricular systole when the two streams were already contaminated.

Another supposition, looking at the case from another viewpoint, may be elaborated as follows: In cases of patent foramen ovale, while a certain amount of leakage takes place at the mid-part of the auricular diastole when the level of the inflowing blood reaches the opening of the foramen, the major portion of the contamination of the arterial chambers with venous blood from the right auricle takes place at the moment of auricular contraction, when the blood, taking the path of least resistance, is forced through the patent foramen; remembering the short interval between auricular diastole and systole, we may assume that, as the arterial blood flows into the left auricle, part of it, owing to the sclerotic condition of the insufficient mitral valve, falls at once into the left ventricle; the remainder is forced into the left ventricle before an intimate admixture with the venous blood of the right auricle has taken place, and, therefore, enters the systemic circulation with only a minimal amount of contamination. This would be further aided by the functional separation of the two chambers as above suggested.

Both of these suppositions are, necessarily, somewhat farfetched, improbable, and weak; the fact remains, however, that compensation of some kind did take place, and, if we cannot assume such an explanation as the foregoing, we are forced to the theory that the pulmonary circulation was always more extensive than the sys-

temic, and was thus enabled to cope with the problem of the excessive aëration necessary to maintain a proportion between the contaminated blood stream of the systemic circulation and the necessities of the tissues.

The examination of the heart apparently furnishes ample evidence upon which to base such a theory.

In the first place, both the right ventricular and right auricular cavities were much dilated. That this was not due to the terminal dilatation of cardiac failure consequent upon the pneumonia and other embarrassment under which the patient labored is evidenced by the marked hypertrophy which is present in the walls of both cavities, showing the condition to have been one of gradual development and long standing, and we have, therefore, in these two factors, the dilatation showing that the chambers contained more than the usual amount of blood, and the hypertrophy evidencing increased work, extremely suggestive indications of an increased amount of blood in the pulmonary circulation. Add to this the marked enlargement of the pulmonary artery and the links in the chain are apparently complete; as this vessel plays but little part in the fetal circulation and only becomes active after birth and the inception of the respiratory function, it must be looked upon as a condition developing after birth and with the growth of the individual.

It may be objected that all of these factors, with the exception of the hyperplasia of the pulmonary artery, might be accounted for as the end-results of the mitral stenosis which was present. It is true that the mitral valve was markedly stenosed and thus offered an obstacle to the passage of any large—we might say the normal—amount of blood; on the other hand, however, the aorta was extremely small, approximately only half as large as normal, and, therefore, was not capable of accommodating any more blood than the amount which the small mitral orifice was capable of admitting; hence, both were decreased in size and an approximate normal maintained between them, so that the actual functional stenosis was reduced to a minimum—a condition further evidenced by the lack of hypertrophy of the right auricle; and these facts, also, are arguments of a lessened systemic circulation.

Assuming, then, an excessive pulmonary circulation, the mechanism of the functional compensation is rather easily imagined.

Beginning with the ventricular systole, we have both ventricular chambers filled with blood, the left containing the normal amount for the individual, as evidenced by the lack of either dilatation or hypertrophy of its walls. Systole occurs and the streams are forced in the usual directions, the lungs receiving a large influx—and we may recall here that the patient was “always more or less inclined to dyspnea”—while never, at any time, exhibiting any other sign or indication of cardiac or valvular defect, which

shortness of breath may be attributed to the large amount of blood which required aëration. Returning, the left auricle receives the inflow from the lungs, which, excessive in amount, necessitates a dilatation of that cavity, and this, it may be recalled, was found at autopsy; the right auricle, however, receives a comparatively small amount of blood, the relatively small incoming stream from the cavæ. This being in auricular diastole, when the auricles are relaxed, immediate admixture of the two streams occurs; but instead of the two amounts being equal, there is a comparatively small amount of venous blood thrown into a comparatively large amount of arterial blood returning from the lungs, which, therefore, diluted the venous blood to an extent sufficient to markedly reduce the element of contamination. Hence, when auricular systole occurs, the left ventricle, instead of receiving (to speak figuratively) a mixture of 50 per cent. venous and 50 per cent. arterial blood, receives a mixture of 80 per cent. arterial and 20 per cent. venous blood—a proportion theoretically containing sufficient oxygen to supply the needs of the tissues, when we remember that the systemic circulation is assumed to be decreased in amount. The dilatation of the right auricle is readily accounted for by the fact that part of the large amount of blood received into the left auricle—to which must be added that leaking in from the right auricle—is forced into the right auricle by the contraction of the left in the absence of the septum.

Such a supposition would also readily account for the dyspnea which would be consequent upon the large amount of blood in the pulmonary circulation, causing a rapid and increased gaseous interchange.

The hypoplasia of the aorta we are utterly at loss to explain the normal condition of its walls seems evidence in favor of the condition being congenital.

The mitral stenosis we believe to be partly congenital, in that the valve was probably never as large as it should have been, and partly due to the original infection from which the patient suffered a year before her death, and following which she eventually developed symptoms which led her physician to make a diagnosis of cardiac disease. The lesions of the tricuspid valve we also refer to the preceding endocarditis, both valvular lesions being chronic in type.

The entire case presents a problem at once puzzling and complex, which is not readily capable of satisfactory explanation, and it is to be regretted that, owing to the stipulation made when permission was given for the autopsy, the specimen could not be preserved for complete and minute examination, and, also, owing to the limited time in which the autopsy was made, that no photographs could be taken.

Had only some suspicion of the cardiac defect been aroused,

electrocardiograms and tracings might have aided in shedding some light on the conditions of the circulation.

We regret that we were unable to search the literature for references to analogous conditions which may have been reported, or to make a careful search for references which might have been of service in the possible explanation of the case; the conditions as found, however, are sufficiently unusual and interesting to warrant some record, no matter how superficial or how unsatisfactory.

We would express our thanks to Dr. Alfred Stengel, in whose service the case occurred, for permission to report it; to Dr. Kenneth M. Lynch, who made the autopsy and was kind enough to go over it with the writer in detail; to Dr. E. R. Samuel, who copied the diagram accompanying the report; to Dr. Allen J. Smith, for facilities extended in the Laboratory of Pathology.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College; assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College. Vol. I, March, 1914. Pp. 406; 25 illustrations. Philadelphia and New York: Lea & Febiger.

THE first volume of *Progressive Medicine* for this year opens with an article on the surgery of the head and neck, by Charles H. Frazier. He takes up in great detail the pineal body, trigeminal neuralgia, and surgery of the auditory nerve. He also devotes considerable space to cancer of the oral cavity. The last part of his article deals with tuberculosis and carcinoma of the mammary gland.

In a 32-page article by George P. Müller, the surgery of the thorax, excluding diseases of the breast, is taken up. Intratracheal insufflation anesthesia, the surgery of the heart, the surgical treatment of tuberculosis, and carcinoma of the esophagus are the most important subjects dwelt upon by him.

Infectious diseases are reviewed by John Ruhräh, who as usual has written an instructive article. In his contribution of 127 pages all the important infectious diseases and many of the rarer ones are carefully discussed, and the most recent views regarding them are set forth.

An interesting contribution on diseases of children is furnished by Floyd M. Crandall. He devotes considerable space to the important subject of infant feeding.

In a short article of 55 pages, George B. Wood has furnished a thorough, careful, and up-to-date review of rhinology and laryngology.

An interesting article on otology has been written by Arthur B. Duel, who takes up the recent advances in this specialty in the course of a 46-page contribution.

This volume adequately maintains the high standard which is invariably found in this excellent work of reference. G. M. P.

A TEXT-BOOK OF PATHOLOGY. FOR STUDENTS OF MEDICINE. By J. GEORGE ADAMI, M.A., M.D., F.R.S., Strathcona Professor of Pathology, McGill University, and JOHN McCRAE, M.D., M.R.C.P. (Lond.), Lecturer in Pathology and Clinical Medicine, McGill University. Pp. 759; 304 engravings and 11 colored plates. Philadelphia and New York: Lea & Febiger.

IN spite of the large number of works on pathology that are obtainable, there has existed for a long time a crying need for a thoroughly up-to-date text-book on pathology in English. The present volume fulfils all the requirements that are essential to a useful and adequate text-book, designed particularly for medical students and practitioners. By the exercise of extreme care and excellent judgment, the authors have accomplished the difficult task of condensing into a single volume of convenient size an unusually complete and thorough, yet clear and concise discussion of the entire subject of pathology. Their long experience as skilled teachers has evidently enabled them to appreciate the needs of the student, for throughout the book non-essentials are omitted, fundamental principles are dwelt on, and those phases of the subject that are of prime importance and which it is imperative for the student to grasp are emphasized and clearly explained.

In Part I the first chapter deals with the morphology, physiology, and chemistry of cells, together with certain other properties of cells and tissues, such as multiplication, adaptations, differentiation, and inheritance. In subsequent chapters the causes of disease and the various morbid and reactive processes, such as inflammations, infections, and immunity, etc., are taken up. The section concludes with chapters on progressive tissue changes as overgrowths, regeneration, metaplasia, etc.; and the tumors and regressive changes which include the degenerations and infiltrations, necrosis and death. The clearness with which certain complicated subjects are handled makes this section on general pathology noteworthy.

Part II deals with special and systemic pathology. In this section the disease processes peculiar to the various organs and systems of the body are discussed. All the chapters in this second part are well done, but the chapters on the cardiovascular system and the urinary system are of particular interest.

As a piece of book-making the volume leaves nothing to be desired, the beautifully clear type and many excellent illustrations add much to the usefulness of the book.

It is not too much to say that Adami and McCrae have written the best text-book on pathology that has yet appeared as a single volume in English. The warm welcome which has uniformly been accorded this work by pathologists, and especially teachers of pathology, was to be expected, and is amply justified by the unusual merit of the book.

G. M. P.

A MANUAL OF SURGICAL TREATMENT. By Sir W. WATSON CHEYNE, Bart., C.B., D.Sc., LL.D., F.R.C.S., F.R.S., Hon. Surgeon in Ordinary to H. M. the King; Senior Surgeon to King's College Hospital; and F. F. BURGHARD, M.S. (Lond.), F.R.C.S., Surgeon in King's College Hospital and Consulting Surgeon to the Children's Hospital, Paddington Green. New edition, entirely revised and largely rewritten, with the assistance of T. P. LEGG, M.S. (Lond.), F.R.C.S., Surgeon to the Royal Free Hospital and Assistant Surgeon to King's College Hospital; and ARTHUR EDMUNDS, M.S. (Lond.), F.R.C.S., Surgeon to the Great Northern Central Hospital, Assistant Surgeon to King's College Hospital. In five volumes: Vol. V, pp. 619; 152 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THIS volume, which concludes the new edition of this useful work, discusses the surgical affections of the pancreas, liver, and spleen; surgery of the neck; surgery of the breast, thorax, and thoracic viscera; surgery of the genito-urinary organs (of the male); and concludes with an appendix, in which an attempt has been made to describe in the compass of less than ten pages "operations on the female genital organs, which may be found necessary in the course of an ordinary laparotomy." This latter phrase implies that in most cases the diagnosis is not made until after the surgeon has "taken off the lid." Such we are sure is not actually the case in King's College Hospital, or in any other hospital served by so able surgeons as the writers of these volumes; but it does seem strange for the authors to describe abdominal hysterectomy for myomata, removal of broad ligament cysts, and the "operation for extra-uterine fetation" as procedures which may unexpectedly become necessary after the abdomen has been opened for chronic appendicitis or some undiagnosed acute abdominal condition. The authors express regret that lack of space forbids them going "more fully into the various conditions of the female genital organs which require laparotomy," because they "are strongly of the opinion that the operation should only be performed by a surgeon who is prepared to deal with any abdominal condition that may be met with, and that no one should open the abdomen who is only able to treat some special organ." This sounds very well, and no doubt is the proper view to take; but it is one which can very easily be pushed too far. Thus one might forbid operations on any part of the female genital tract by those not qualified to treat any condition that may be met with in that tract; he might do the same for the male genito-urinary tract, and permit no one to perform a circumcision unless he were equally qualified to do a nephrectomy or at least a prostatectomy; he might forbid anyone to operate for a wen of the scalp, or to trephine in a case of depressed fracture of the skull, unless he were also competent to extirpate the Gasserian ganglion or remove a brain tumor. This clearly is

a *reductio ad absurdum*; but the principle holds good, and it is no more blameworthy for a "gynecologist" to feel a Hallerian diffidence about undertaking a partial gastrectomy or even a choledochotomy should he unexpectedly meet with a state of affairs rendering these operations proper, than it is for an "abdominal surgeon" to be overwilling to invade the pelvis when he has not sufficient skill to make in advance a reasonably correct diagnosis in the presence of an obscure condition in which the pelvic organs may be involved.

Affections of the male genital organs are discussed at a length of 167 pages, and 168 pages are devoted to the surgery of the bladder and kidneys. It certainly seems that these sections might have been curtailed with advantage if more room could thereby have been gained for the surgery of the female genitals, since in the average general surgeon's experience the latter occupies a much larger and more important place than genito-urinary surgery.

The other divisions of the book, dealing with abdominal and thoracic surgery, and affections of the neck, leave little to be desired. Perhaps a little more of the "newer surgery" of the thorax might have been included; a fuller description of the difficulties often encountered in choledochotomy in the absence of the gall-bladder would have been desirable; and it might have been well at least to mention that many surgeons now begin the operation for carcinoma of the breast by the axillary dissection, and that most of them deem it imperative to remove the pectoralis minor as well as *all* of the pectoralis major in every case.

On the whole, the volume can scarcely be said to equal those which have preceded it; but taken all together they form a most convenient and useful work of reference.

A. P. C. A.

A TEXT-BOOK OF THE PRACTICE OF MEDICINE. By JAMES M. ANDERS, M.D., LL.D., Professor of Medicine and Clinical Medicine, Medico-Chirurgical College, Philadelphia. Eleventh edition, pp. 1335. Philadelphia and London: W. B. Saunders Company, 1913.

DOCTOR ANDERS' text-book needs no further recommendation than to say that this the eleventh edition is fully up to the standard of the previous ten editions that have appeared from time to time in the past seventeen years. One criticism might be made, that there is included in the text additions that have not as yet been carefully tested, so that some of them already have proved to be fallacious. Another change that it is hoped will be found in the next edition, is a revision of the sections upon lithemia and intestinal auto-intoxication. These are but minor points, however, that are truly obscured by the general excellence of the whole book.

J. H. M., Jr.

ANATOMY, DESCRIPTIVE AND APPLIED. By HENRY GRAY, F.R.S.. Fellow of the Royal College of Surgeons; Lecturer on Anatomy at St. George's Hospital Medical School, London. A new American from the eighteenth English edition; thoroughly revised and reëdited, with the Basle Anatomical Nomenclature in English. By ROBERT HOWDEN, M.A., M.B., C.M., Professor of Anatomy in the University of Durham, England. Pp. 1407; 1126 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

It is scarcely necessary to advertise or review the successive editions of Gray's *Anatomy*. There never was such a book, and "none but itself can be its parallel." This edition, from the eighteenth English edition, has been edited by Howden, and is, we believe, the most satisfactory edition of Gray's *Anatomy* now on the market. The bulk of the volume has been reduced by about 200 pages, and this appears to have been accomplished by condensation rather than by omission. The histology of the elementary tissues and general embryology are discussed at a length of 160 pages at the beginning of the volume, rendering this portion of the work more useful for the student and handier for reference than when as in former editions these sections were scattered throughout the volume. The histology of more highly specialized tissues is considered along with the organs to which they are specially related.

The sections on surface anatomy have also been assembled, and are placed at the end of the volume, where this important subject may be studied without paging through the entire book.

Especially valuable, as in all editions of Gray, are the paragraphs on applied anatomy, appended to each section of the work. All of these are admirable in conciseness and lucidity, and most of the operations described truly represent modern surgery; but one is amazed at the barbarous method of panhysterectomy recommended at page 1254.

The Basle Anatomical Nomenclature is given in English, but whenever this necessitates a marked change in terminology the old terms, so long familiar, are also given in brackets. Especially in the nervous system are the advantages of this terminology apparent; in a former edition of Gray the task of ascertaining what the editor of the section on neurology was talking about was far too great for the average intellect. The editor is so careful, moreover, that he gives a complete Glossary of the Basle Anatomical Nomenclature at the end of the volume, so that any uncertainty as to meaning which may arise may be quickly dissipated.

Many new illustrations (about 200 in all) have been added, many of them replacing those in former editions, but a number of them are additional. Though the total number of illustrations has been decreased from 1149 in the edition of 1908 to 1126 in

the present edition, many of the figures in the former edition can well be spared: they were not worthy of Gray. These new illustrations, however, are of the highest type, many of them being in colors. Among the best of the latter are illustrations of the joints, of surface anatomy, of the abdominal organs, and of the lymphatics.

Constant use of the book serves to confirm the publishers' statement that "as a teaching instrument the new Gray's *Anatomy* embodies all that careful thought and unstinted expenditure can combine in a text-book."

A. P. C. A.

A TEXT-BOOK OF PHYSIOLOGY. FOR MEDICAL STUDENTS AND PHYSICIANS. By WILLIAM H. HOWELL, Ph.D., M.D., Professor of Physiology, Johns Hopkins University, Baltimore. Fifth edition. Pp. 1020; fully illustrated. Philadelphia and London: W. B. Saunders Company, 1913.

THE first edition of this admirable book was so excellent in plan and execution that subsequent editions have brought about fewer changes than would be expected if the great strides in physiology alone were considered. Substantial physiology, the kind which will stand the test of time, was presented in a most lucid form. It is true that some material found its entrance which required further verification, but the author here was extremely careful in its discussion, emphasizing the shortcomings of the available material. As subsequent evidence accumulated the additions or subtraction which were necessary involved comparatively little space. Thus, the fundamental basis of the book was so excellent that new editions required comparatively few changes. The new discoveries have been weighed properly and conservatively by the author and not introduced unless well established and of value to the student and practitioner. Consequently, we are not surprised to find that the present edition has not exceeded the preceding in size, and that many pages remain absolutely unaltered. Nevertheless, as we page through the fifth edition and compare it with its predecessor we note that the author has a splendid command of the new unfoldings which have come to light in the last two years, the period which has elapsed between these two editions.

The greatest number of changes occur in the chapters on digestion and metabolism. The work of Hewey and Bensley on the origin of hydrochloric acid is given brief notice, and that of Stone and Bernheim which may throw some light upon the fatal effect of high intestinal obstruction in man. The text has received considerable recasting in the discussion of the fate of the absorbed products of digestion, particularly that of protein. In this connection the vitamins receive their just due. The recent work on the reductions and oxidations in the body are also referred to with perhaps sufficient emphasis.

The chapter on the internal secretions has also undergone important revision, the suprarenals are given more space in their consideration, the work of Cushing in connection with the pituitary body is referred to, as are also the interesting observations of Steinach upon the internal secretions of the testicles. The chapters on reproduction and secretion also show evidence of careful attention although the changes are comparatively few.

The edition will undoubtedly find the continued favor which the preceding editions have had.

E. L.

EARLY PULMONARY TUBERCULOSIS: DIAGNOSIS, PROGNOSIS, AND TREATMENT. By JOHN B. HAWES, 2d, M.D., Assistant Visiting Physician, Director Tuberculin Department, Massachusetts General Hospital; Secretary, Board of Trustees Massachusetts Hospitals for Consumptives. With Preface by RICHARD C. CABOT, M.D., Assistant Professor of Medicine, Harvard University. Pp. 114; 45 illustrations. New York: William Wood & Co., 1913.

THE salient features of early pulmonary tuberculosis have been much dwelt upon and may all be found somewhere in the vast literature of tuberculosis, but nowhere can they be found so conveniently grouped or stated with such conciseness and authority as in this small book. Particularly well fitted for the task by reason of careful training and large experience, Hawes has handled this vital subject with rare judgment, and has emphasized its importance with effectiveness the more telling because of the terse, epigrammatic style in which he writes. Such a sentence as, "If the stethoscope were used less and the thermometer more, fewer mistakes would be made" well illustrates how he drives home an important point.

The book deals solely with the problem of *early* tuberculosis, and particularly its diagnosis. The various facts that should be especially considered in the history of such patients are first taken up. Hawes then discusses the signs and symptoms that should be noted in these cases. His sixth chapter, on the adventitious signs in the chest not due to tuberculosis, but often mistaken for evidence of pulmonary disease, and the tenth chapter on conditions which may simulate tuberculosis are worthy of note. In addition, he discusses the value of tuberculin and the x-rays in the early diagnosis of tuberculosis, as well as bronchial gland tuberculosis in children, the prognosis and course of early tuberculosis, and its treatment. The book concludes with five appendices in which are given the histories of illustrative cases, a reliable method for staining tubercle bacilli in sputum, photographs and x-ray pictures of characteristic types of chests, data in reference to the Massachusetts tuberculosis

sanatoria, and finally valuable directions for living and sleeping in the open air.

The book is obviously the work of one so thoroughly master of all the details of the subject, as well as its literature, that he is capable of stating with refreshing frankness and assurance the most reliable modern views in regard to tuberculosis.

The book was written for a definite purpose, namely, to help the general practitioner, and it should well fulfil its mission. No one who reads it thoughtfully can fail to receive from it a clearer conception of the value and importance of the early diagnosis of pulmonary tuberculosis.

G. M. P.

STAMMERING AND COGNATE DEFECTS OF SPEECH. By C. S. BLUEMEL. 2 Vols. Pp. 741. New York: G. E. Stechert & Co., 1913.

THIS work should have been called "A Theory of the Basic Cause of Stammering," as clinical cases supporting the author's views are not cited and the method of cure is a proposition without verification, sketched in its broadest and most general aspect.

The work is published in two volumes, the first volume is an orderly presentation of subjects germane to stammering—psychological considerations, brain localization, aphasia, the mental condition of the stammerer, and the different forms of stammering, with a short final chapter on the author's principles of treatment. It must be said that this is done so well, and with such evidence of study shown by interesting quotations from Bastian, Galton, James and others, that it is worth reading.

The author's contention is that "pure stammering" is altogether mental and is due to weak auditory memory—a transient auditory amnesia. Other possible elements in the cause (fear, bewilderment, inhibition of the will from auto-suggestion, perversion of the verbal imagery) are secondary complications.

The method of cure advocated, and to the author the only scientific and effectual one, is the supplementing of the weak inert auditory imagery by visual and kinesthetic imagery. In other words, the stammerer memorizes by observation and practice the proper muscular movements to produce the desired sounds. He then produces the desired sound, or at least starts it, by pure muscular memory. This method, as we all know, is the one used in teaching the congenital deaf to speak.

The second volume discusses the different principles on which various treatments for stammering have been based—respiratory exercises, vocalization and vowel production, articulatory modes of enunciation, mechanical appliances, and psychological methods.

Altogether the book is well worth reading and a very valuable contribution to the subject.

W. S. C.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Etiology of Variola and Vaccine.—E. PASCHEN (*Deutsch. med. Woch.*, 1913, xxxix, 2132) presents the evidence thus far collected which tends to show that the bodies which he has been studying for a number of years are in reality the causative agent of variola and vaccine. The bodies are very small, round, sharply defined, coccus-like objects, which divide directly. On many of these bodies one can see a very delicate, filamentous process. Frequently the bodies are found in pairs, which are united by a filament; this appearance is even more striking with dark field illumination. The two bodies seem to dance about, approaching and receding from one another. As von Prowacek has shown, this is Brownian movement. Often there is a halo surrounding the bodies. It has been demonstrated that they pass through the Berkefeld filter. They are stained with difficulty, but satisfactory preparations may be obtained by first treating with Loeffler's mordant and then staining with carbol-fuchsin, carbol-gentian violet or carbol-methyl violet. The intensity of the staining is influenced by the apparent size of the bodies and also by the thickness of the surrounding layer of serum. There is considerable variation in size, but the largest of the bodies are less than 0.5 micron in diameter. With Giemsa's mixture, they are stained faint blue and are easily decolorized. The bodies are chiefly intracellular; after inoculation they enter the epithelial cells and multiply rapidly in them. They are very resistant; they are not dissolved by 2 per cent. potassium hydrate, 2 per cent. acetic acid, chloroform, alcohol, ether, distilled water, or physiological salt solution. They are agglutinated by specific immune serum. In the lesions of other skin affections, the bodies found in variola and varicella have not been discovered.

Experimental Hyperglycemia in Man through Intravenous Injections of Sugar.—S. J. THANNHAUSER and H. PFITZER (*Münch. med. Woch.*, 1913, lx, 2155) have attempted to shed new light on sugar metabolism by studying the effects of intravenous injections of glucose in health and disease. For the determination of glucose in the blood they have employed Bang's method, which is accurate with minute quantities of blood. They have determined the blood glucose before the injection, when half of it had been administered, and at the completion of the injection. Determinations were also made every five minutes for the first quarter of an hour after the injection, then after one, four, and twelve hours had elapsed. Thannhauser and Pfitzer employed a 7 per cent. solution of glucose which had been carefully pasteurized; they injected 500 c.c. of this intravenously, equivalent to 35 gm. glucose. The normal individual excretes a trace of sugar in the urine after the intravenous injection of 20 gm. glucose. As in alimentary or subcutaneous administration of glucose, a marked increase in the amount administered produces only a slight increase in the sugar in the urine (0.1 gm. to 0.5 gm.). Thannhauser and Pfitzer find that the quantity of blood sugar reaches the normal level in one-quarter of an hour after the injection. Here hyperglycemia leads to glycosuria. In patients suffering with disease of the liver (lues, metastatic cancer, cirrhosis), the conditions were found to be quite different. The glucose excreted in the urine (0.5 to 3 gm.) is only slightly greater than in the normal, but the hyperglycemia persists for hours without glycosuria. In chronic nephritis, in which blood glucose is usually in excess of the normal, there is a sharp rise in the blood sugar curve with a return to the previous level within one quarter of an hour and only a slight glycosuria (0.2 to 0.44 gm.). In severe diabetes all of the injected sugar is excreted in the urine; the increased percentage of blood-sugar caused by the injection is maintained for several hours. The carbohydrate depots are apparently unable to warehouse the excess. In mild diabetes the findings are similar to those in normal individuals.

The Benzol Therapy of Leukemia.—E. MÜHLMANN (*Deutsch. med. Woch.*, 1913, xxxix, 2083) utters a word of warning regarding the use of benzol in the treatment of leukemia. He reports the findings at autopsy in a patient with lymphatic leukemia treated with benzol, the amount given varying from 0.25 to 3 gm. daily, with intermissions of a few days occasionally. At autopsy there were found liver necroses affecting the central parts of the lobules. Since Neumann has reported similar findings in the liver in a patient with myeloid leukemia treated with benzol and as hepatic injury is frequent in animals which have been given benzol, Mühlmann thinks it very likely that the hepatic lesions in his patient and in Neumann's case are attributable to the benzol. He urges caution in the employment of this drug.

Thymin in the Treatment of Exophthalmic Goitre.—R. HIRSCH (*Deutsch. med. Woch.*, 1913, xxxix, 2141) finds, as do most observers, that Basedow's disease is very rare in childhood. Furthermore, she observes, children are very tolerant of preparations of the thyroid gland. These considerations led her to try the administration of thymus gland to patients suffering with hyperthyroidism. Thymin,

manufactured by Poehl, is the preparation used. Two tablets of 0.5 gm. have been given daily. Hirsch has tried this treatment in 12 cases and says the results have been quite encouraging. Details of cases are reserved for a later contribution. She finds that thymin has an elective action on cardiopathies of thyreotoxic origin. As she noted that the sleep of patients with hyperthyroidism is much improved by administration of thymin, she has employed it as a hypnotic. Hirsch administered it for this purpose first to two patients with diabetes insipidus (Wassermann reaction negative in each case). The sleep of each patient had been disturbed by the necessity of drinking water and urinating frequently. One tablet was given in the morning and two at night. After instituting this treatment, both patients promptly began to sleep through the entire night and other symptoms were also improved. Two tablets at night have produced restful sleep in neurasthenics.

Observations on the Blood Sera of Gouty Individuals.—E. EHLMANN and H. WOLFF (*Münch. med. Woch.*, 1913, lx, 2115) have made observations on the uric acid content of the blood of normal and gouty subjects. They summarize their findings as follows: (1) On a purin-free diet the blood serum of normal individuals contains sufficient uric acid to estimate quantitatively. (2) Cases of typical gout on a purin-free diet present the same (or lower) values for uric acid as the normal sera. (3) Therefore, determination of the uric acid in the blood serum is of no value in the diagnosis of atypical gout. (4) A few hours after the administration of atophan the uric acid of the blood is unchanged; in one instance it became so low that it could not be determined. In an acute attack of gout, during the administration of atophan, the uric acid was much lower than it was a few days later. (5) Uric acid is practically always more abundant in the blood serum than the purin bases, contrary to Wiechowski's findings with whole blood. (6) The hydrogen ion concentration is much higher in gout than normal and also higher than in diabetic coma. This indicates a decreased alkalinity of the blood in gout. (7) In some cases of gout a lipemic appearance of the blood was noted.

Further Studies on Experimental Syphilis.—P. UHLENHUTH and R. MULZER (*Berlin. klin. Woch.*, 1913, xlix, 2031) report further studies on experimental syphilis which throw additional light on the pathology and therapy of the disease. Uhlenhuth and Mulzer summarize their results as follows: (1) In latent syphilis (positive Wassermann without clinical evidence of the disease) they have not yet succeeded in demonstrating the infectivity of the blood through inoculation of a rabbit's testicle. (2) Animal inoculation does not furnish conclusive evidence of the efficacy of therapy. (3) Positive inoculation experiments with the blood of patients showing the signs of tertiary syphilis have been obtained, though this seems not to be the rule. (4) The inoculation of the blood of patients exhibiting signs of a late hereditary syphilis (gummas, keratitis, positive Wassermann) has invariably given negative results. (5) A number of inoculations of the saliva and the urine of patients suffering with a recent lues have thus far given negative results. (6) In a recent case Uhlenhuth and Mulzer have again been able to demonstrate the infectivity of the semen.

They have also succeeded again in showing that the milk of a mother free from symptoms, who had given birth eight days previously to a syphilitic infant, was infectious to the rabbit. (7) The blood as well as bits of tissue from the eruptions of a patient suffering with "malignant" lues, when inoculated into rabbits, almost invariably produced a syphiloma of the testis rich in spirochetes. (8) The spinal fluid of 2 recent cases was shown to be infectious. (9) Blood and spinal fluid of tabetics and paralytics have always given negative results on inoculation. (10) In one case they succeeded in producing a typical lesion in the rabbit's testicle by inoculation of a suspension of the brain of a paralytic. (11) Liver and spleen of syphilitic rabbits seem to be more infectious than the other internal organs. (12) Dilutions of 1 to 1000 (2 c.c.) of the usual syphilitic testicle emulsion may give positive results on inoculation.

Experimental Syphilis of the Nervous System.—A. JAKOB and W. WEYGANDT (*Münch. med. Woch.*, 1913, lx, 2037) report observations on the histology of the nervous system of rabbits infected with syphilis. They find that experimental syphilis, like the human infection, leads to a wide dissemination of the spirochetes in the body. Both the central and the peripheral nervous systems are affected relatively early; frequently there is meningeal involvement. In all the experimental animals severe inflammation and infiltration are seen; these changes originate in the mesodermal coverings or in the bloodvessels of the entire nervous system. By extension the nervous parenchyma becomes involved. The cells concerned in the infiltrative process are chiefly lymphocytes, plasma cells, and polyblasts. Of particular interest are the localized processes. These may consist of granulation tissue with large numbers of plasma cells, both in the peripheral and central nervous systems, with tumor formation, or there may be a localized collection of plasma cells in the neighborhood of a markedly infiltrated vessel which has led to severe degenerative and proliferative changes in the contiguous nervous tissue.

SURGERY

UNDER THE CHARGE OF

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The Removal of Ascites.—KUMARIS (*Zentralbl. f. Chir.*, 1913, xl 1916) removes as much as possible of the parietal peritoneum in order to produce abundant adhesions between the viscera and abdominal

wall. The absorptive capacity of the peritoneum removed has very probably been diminished, and after the operation the direct escape of the fluid is more easy. The eventual, extensive adhesions between the viscera and the extraperitoneal tissues gives rise to an abundant collateral circulation. This is supplied particularly by the omentum, but all the other organs contribute. Kumaris reports the following case, illustrating the application of the method: A woman, aged fifty years, suffered from malarial ascites, for which it was necessary to withdraw the fluid by puncture every fifteen days. The circumference of the trunk at the umbilicus was 110 cm., and there was edema of the ankles. Forty-eight hours after removal of the fluid by puncture a 19-cm. incision was made in the median line above and below the umbilicus. The liver and spleen were contracted and rough. On each side of the incision a strip of the silver white and thickened peritoneum, 25 cm. by 25 cm., was removed. The omentum was fixed to this surface by two sutures. Layer sutures of the abdominal wound were employed. Forty-eight hours after operation the limbs showed a "dry skin," and the swelling had disappeared. This did not follow the previous punctures. Eight days after the operation the circumference of the trunk was 85 cm., and fifteen days afterward 80 cm., while the general condition was good. Unfortunately on the following day there developed a very severe erysipelas of the face and the patient died twenty-two days after operation. The abdomen was then soft and contained only a small quantity of fluid and had a circumference of 80 cm.

The Diagnosis of Dislocation and Fracture of the Semilunar Cartilages.—AARAU (*Zentralbl. f. Chir.*, 1913, xl, 1852) says that sometimes the symptoms are completely negative, so that the operative indication rests upon an exact history. In such cases Aarau has found a systematic auscultation of the knee-joint of advantage. There is no sound characteristic of an injured meniscus. In some clinically evident cases, at the moment when the injured cartilage is torn from its place, a rather loud cracking sound is heard. It is in such cases that the meniscus is torn from its attachment in a large extent and sometimes is completely separated. It is much more difficult to diagnose those cases in which the meniscus is only partly torn away and which give only few clinical symptoms. In these a comparative auscultation of both knees will bring out a difference in sound. On the unaffected side little or no sound will be heard. Even on strongly forced movements only a slight cracking sound will be detected here and there. On the affected side, whether the internal or external meniscus be involved, by slow movements, a rubbing sound, and by extensive and forced movements, a cracking sound is perceptible. Sometimes a very loud sound is heard. It is louder on flexion than extension. In 6 out of 7 cases operation established the diagnosis thus made. Auscultation is best made with both ears by a stethoscope, the bell of which is provided with a rubber ring to overcome the effect of the uneven surfaces about the knee. Auscultation should be tried in the standing position with marked flexion of the knee, as well as in the recumbent position. The joint-space on both sides of each joint should be ausculted and the differences noted.

Sun-treatment of Tuberculosis of the Foot.—LEUBA (*Deutsch. Zeit. f. Chir.*, 1913, exxv, 413) gives a *resume* of the results of the exposure of tuberculous feet to the sun, in Rollier's clinic. The patient is first confined to bed and for a time (three to fifteen days) is constantly exposed to the sun all morning, different portions successively until the whole body has been covered. By gradually increasing the extent of the exposure finally the whole body is exposed at one time. In a similar manner the time of exposure is gradually increased until finally the patient can remain exposed for four hours at a time, without disturbances of the skin, the nerves, or the heart. The treatment of the foot is as follows: The affected foot is placed on an even surface, so inclined that the foot is higher than the pelvis. The tendency to the equinus position is combated by the use of a removable plaster splint which permits mobilization. The sinuses are exposed to the sun without any dressing, and to the free air in the absence of sunshine. At night they are merely covered with compresses. No injections nor operations are employed. When healing is obtained, as demonstrated by the *x*-rays, the patient returns to his home and for at least a year wears an apparatus by means of which the support is taken at the knee and the patient places no weight on the recently healed foot. The combination of the fresh air and sunbath produces a return of strength in the whole organism, which is essential for the cure of surgical tuberculosis. These patients with their bronze-colored skin, which remains uncovered for the greater part of the day, are resistant to changes in the temperature. The fever usually falls rapidly, the appetite increases, digestion regulates itself, and the respiratory capacity is improved. The hemoglobin index is frequently greater than normal. Locally the pain disappears and the swelling and contractures are much relieved. Fistulae and granulation tissue gradually diminish and sequestrae are separated. Abscesses may be absorbed but it is best to remove the pus by punctures. Tuberculous joint affections exposed to the sun heal without atrophy and often without ankylosis.

Acute Hemorrhagic Pancreatitis.—RUNGART (*Deutsch. Zeitsch. f. Chir.*, 1913, exxv, 530) studied 7 cases from Tilmann's clinic. In all of the cases there was the sudden development of the severe symptom-complex, the malignant and stormy course of the whole process and the characteristic relation between the pulse and temperature. Most of the cases began with a severe pain in the upper abdomen and a simultaneous cessation of intestinal activity. From a previous excellent general condition, they pass rapidly, in a few hours, into a severe condition of collapse with a striking incongruence between the temperature and pulse. The temperature generally remained about normal while the pulse mounted to 120 and higher and was small and soft. All but one of his cases died. All authors agree now on the necessity for early operation in order to drain the extravasated pancreatic secretion, and the discharge from the necrotic tissue. The best method of drainage varies with the type of case. Those in which the symptoms present, chiefly, anteriorly, should be drained by the transperitoneal route with splitting of the capsule, sponging away the exudate and applying a tampon over the gland. In the dorsal form

drainage should be provided from the flank or back by a retroperitoneal tampon. The main point is to decide upon operation in every case, even in those in which the presence of pancreatitis is only suspected. In the great majority of cases an exact diagnosis cannot be made until the best time for operating has passed. It is in such cases that exploratory laparotomy has its best justification. A troublesome fistula frequently follows operation. Wohlgemuth has shown that a diet with the carbohydrates decreased or absent and with the avoidance of acids, will cause a considerable decrease of the pancreatic secretion which makes the fistula troublesome.

Deaths from Anesthesia and Lessons to be Drawn from Them.—COTTON (*Annals of Surgery*, 1913, lviii, 934) says that the fact that he or any surgeon can report 10 deaths and 3 close approaches to death from anesthesia personally observed in the course of two or three years, is of itself evidence that the old delusion of the safety of anesthesia can no longer be maintained. It has been maintained in the past, charging off to shock, heart failure, intercurrent pneumonia, alcoholism, etc., the great majority of cases that we ought not honestly regard as due to anything but anesthesia. Perhaps the propriety of classifying some of his list of cases as anesthetic deaths may be brought into question, but if they had not been anesthetized the trouble would not have occurred. We should have none but really skilled anesthesiologists. This is not yet possible, but we must keep hammering at the kind of anesthesiologists we have. One of his deaths was probably from acid intoxication, and in another failure to recognize and treat acidosis would, he believes, have lost the case. Often, no doubt, it is not important, if present, but it is well to bear in mind, and in case of doubt, sodic bicarbonate and early feeding by mouth or rectum is harmless and may change the issue entirely. Cotton bars absolutely any chloroform mixture as a preliminary. At best it calls for very expert handling, and he sees in practice few cases requiring its use. Intratracheal anesthesia is for the man who knows how. Cotton's preference is for the gas-oxygen-ether combination.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Leukemia with Benzol.—BARKER and GIBBES (*Johns Hopkins Hosp. Bull.*, 1913, xxiv, 363) describe briefly the results of benzol therapy in cases of leukemia and allied blood diseases which have been reported by various observers. They note a total of 18 cases from the literature, of which number 13 were cases of

spleno-myelogenous leukemia and 2 were lymphatic leukemia. Barker and Gibbes add a case of spleno-myelogenous leukemia that responded very favorably to benzol therapy. The course of benzol administration extended over approximately eleven weeks, during which period the total number of white blood cells returned to normal, the red blood cells increased from 3,600,000 to 5,000,000, with a corresponding increase in the hemoglobin content from 65 per cent. to 82 per cent. While their patient progressed in a satisfactory manner with benzol alone, they feel that the possible value of other accessory measures, such as x-rays, arsenic, thorium-X, and radium, in the therapy of leukemia should be kept in mind. Pappenheim's criticism of the benzol treatment, based upon a theoretical consideration of Selling's work and an attempt to apply some experimental studies has been replied to by von Koranyi. The latter author believes that the toxic manifestations in rabbits produced by relatively immense doses of benzol do not imply that similar effects follow upon the use of the drug as it is now therapeutically employed in leukemia. The ultimate place of benzol in the treatment of leukemia, polycythemia, and Hodgkin's disease can be determined only through further studies which include careful clinical observations. Barker and Gibbes emphasize the facts, first, that benzol does possess dangerous toxic properties; second, that its clinical effects are not yet clearly understood, and, third, that the greatest care should be exercised in its administration. A studious regard for the dosage as thus far determined, a watchfulness for the manifestations of poisoning that are well defined and easily detected, and a willingness to employ other measures in conjunction with this drug are means that will serve to give the new treatment a fair trial and prevent its falling into an undeserved disrepute. No patient should be treated by benzol unless he can be kept under continuous close observation; for the present, therefore, it may be well to restrict its use to the treatment of patients in hospitals.

The Action of Nitrites and Drugs of the Digitalis Group on the Isolated Coronary Artery.—VOEGTLIN and MACHT (*Jour. of Pharm. and Exp. Therap.*, 1913, v, 77) relate their observations as to the effect of certain drugs upon the isolated coronary artery with particular reference to constrictor or dilator action of the drugs studied. They found that digitonin and digalin produce relaxation, while digitoxin, digitatin, and bufagin cause a constriction of the coronary arteries. Digitonin is probably responsible for the dilatation produced by digalen and the infusion of digitalis. All the nitrites were found to produce prompt relaxation. It was also found that the nitrites and digitalis-like bodies, can antagonize each other in their action. Voegtlin and Macht believe that the action of these drugs is similar on the intact mammalian heart and, therefore, whenever coronary spasm is to be avoided or guarded against, it would be advisable to employ the digitonin-containing preparations, or to simultaneously administer the nitrites. Furthermore, if angina pectoris is due to spasm of the coronary vessels, they believe their results explain the favorable action of the nitrites in coronary angina.

Vaccination against Varicella.—KLING (*Berlin. klin. Woch.*, 1913, I, 2083) vaccinated children with material derived from the pustules of children with varicella in an institution where there was exposure to the disease in an epidemic form. There was a positive response to the vaccinations in 58 cases where this procedure was applied. In the portion of the institution chiefly affected by the epidemic there were 95 children. Only 1 out of 31 vaccinated children developed the disease, while over two-thirds (44 out of 64) of those not vaccinated had typical varicella. The technique of the procedure is very similar to that of vaccination for smallpox. On the eighth day after the inoculation, one or usually several red papules develop that become vesicular within twenty-four hours. The vesicles are surrounded by a reddened area that increases in extent for two or three days. On the third or fourth day the vesicles dry up and in two and a half weeks the scab drops off. The general assumption that varicella is harmless and amounts to no more than a contagious skin disease is, according to Kling, very often false, and especially false in institutions where it may develop into a malignant form. Erysipelas and general septicemia may originate from secondary infection of the pustules, while pneumonia, nephritis, extensive gangrene of the skin are complications that are not rare in institutional cases.

The Effects of Emetine on Abscess of the Liver.—SPITTEL (*British Med. Jour.*, 1913, 2756, 1058) reports a case of probable amebic abscess of the liver treated by a combination of subcutaneous injections of emetine hydrochloride and surgery. This patient died, not from the liver abscess, but from too early removal of drainage tubes and subsequent infection of the peritoneal cavity. The noteworthy facts of this case were that the cavity in the liver, which at the time of operation contained one and a half pints of pus, was found nine days later to have a capacity for only four ounces, while a very rapid advance of fibrosis was proceeding throughout the abscess wall. Several separate foci of pus had been rendered inert and showed microscopically the beginning of fibrosis. Spittel believes that mere evacuation of pus and local treatment could not account for this result even if they did for the former. Spittel notes that Rogers has recorded a case in which encystment of a small liver abscess occurred under emetine. Spittel says that in future he will give preference to Roger's method of dealing with liver abscesses—namely, to aspirate them, inject emetine hydrochloride (1 grain to 1 ounce of water), before withdrawing the cannula, sealing the puncture with collodion, and repeating the procedure on a future occasion if required.

The Therapeutic Use of Camphor.—LEO (*Münch. med. Woch.*, 1913, Ix, 2397) experimentally was able to protect mice against pneumococcus infections by subcutaneous injections of saturated solutions of camphor in water. He believes that camphor is able to kill pneumococci in the blood besides acting as a respiratory and cardiac stimulant. Leo gave the camphor solution in doses of 5 c.c. per kilogram of body weight in his animal experiments, but as this dosage produced muscular twitching he advises smaller proportional doses for its use in human beings. For this purpose he recommends a satu-

rated solution of camphor in Ringer's fluid, giving from 150 to 200 c.c. to patients having an average weight of 60 kilos. A saturated solution of camphor in Ringer's solution is equivalent to 0.142 gm. camphor per 100 c.c., and therefore these doses correspond to from 0.21 to 0.28 gm. of camphor. He quotes Lenzmann who has given 75 c.c., corresponding to 0.1 gm. camphor intravenously. No bad effects such as pain, infiltration, or thrombosis have been observed with the intravenous use. He constantly found an increase of blood pressure equivalent to 20 to 30 mg. of mercury as a result of these intravenous injections of camphor solutions. Leo says that Weintrand has also used intravenous injections of a 0.1 per cent. camphor solution, giving from 250 to 350 c.c. with no untoward local or general effects. He advocates the use of such a solution in place of the usual infusion of normal saline.

The Etiology and Vaccine Treatment of Hodgkin's Disease.—BILLINGS and ROSENOW (*Jour. Amer. Med. Assoc.*, 1913, lxi, 2122) confirm the findings of Bunting and Yates and Negri and Mieremet, who described a bacillus that they cultivated successfully from the lymph nodes in Hodgkin's disease. Billings and Rosenow were able to isolate such a bacillus from the lymph nodes in 12 cases of Hodgkin's disease. They treated these cases with autogenous vaccine except in one patient, who received the vaccine prepared from other patients. The vaccine was first given in the dose of from 5,000,000 to 10,000,000 and gradually increased to a maximum of 100,000,000. The vaccine was given subcutaneously and repeated every five to seven days. They have not used it intravenously, but have considered that method of application in obstinate and extreme conditions. In febrile patients the second or third dose has been associated with a reaction consisting of a rise in temperature (in one patient to 107° F.), rapid pulse, and general weakness and discomfort. In non-febrile patients only slight general reaction may occur with a rise of one or two degrees of temperature, slight general muscular aching and debility. In addition to the vaccine treatment they used Röntgen treatment in the majority of the cases treated. Billings and Rosenow state that in 6 of the hospital patients there was a uniform and relatively rapid decrease in the size of the lymph nodes, one of these without Röntgen treatment. One patient treated out of the hospital with the vaccines alone, with very large lymph nodes, markedly enlarged spleen and febrile, had a violent general reaction with the third dose, then became afebrile, and the swellings of the lymph nodes and splenomegaly rapidly diminished. Reports from physicians on two of this series show favorable progress with gradual diminution of the lymph nodes and general improvement. Two of the series died; one with marked enlargement of the mediastinal lymph nodes died soon after the third vaccination and the other, also with involvement of the mediastinal lymph nodes died from the result of mediastinal pressure after only one autogenous vaccination. One patient is apparently cured. There are no palpably enlarged lymph nodes; the formerly much enlarged spleen is no longer palpable; the blood picture is normal; his weight and strength are normal. Billings and Rosenow present this communication as a preliminary note with the hope that the clinical study may be carried on by others.

PEDIATRICS

UNDER THE CHARGE OF

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A Case of Rabies.—ALFRED HAND, JR. (*Archives of Pediatrics*, 1914, xxxi, 9) reports a case of rabies in a boy, aged nine years. The boy was severely bitten in the face by a dog. Pure carbolic acid, followed by alcohol was applied and the wounds dressed with gauze wet with a 1 to 1000 solution of bichloride. The next day the wounds were unusually inflamed and the boy complained of soreness of the jaws and difficulty in swallowing. The parents refusing the Pasteur treatment, the boy was not seen again until he was admitted six weeks later with headache, pain in the throat, and convulsions, during which, however, he did not lose consciousness. The boy developed a continuous activity, lying down, sitting up, and jumping from side to side. The face was flushed a light red and the pupils were widely dilated. There was spasm of the pharynx, and the saliva could not be swallowed but was spat out at intervals of a few seconds. The saliva consisted of small, sticky pellets floating in a watery secretion, which filled a pus-basin in a few minutes. Hypodermics of morphine had no effect on the spasm, but spraying the nasopharynx with a cocaine solution gave immediate relief. The boy took water into his mouth but was unable to swallow it. The body temperature was 106° F., but it was impossible to apply sponge baths owing to the excitement they produced. Later the paroxysms became less acute and there was perspiration, while the pupils again reacted to light, but the boy failed to respond to questions asked, as before. The parents removed the boy to his home, where he died fifteen minutes after his arrival. The boy's brain, examined by the State Livestock Sanitary Board, showed one ganglion cell containing three Negri bodies. One of the rabbits inoculated subdurally with the tissue died subsequently, and microscopic examination of the hippocampus revealed Negri bodies in large numbers. The diagnosis of rabies was made conclusively.

Edema in Infants.—HENRY DWIGHT CHAPIN (*Archiv f. Pediatrics*, 1914, xxxi, 5) reports a series of cases in which the symptoms were studied in their relation to edema. He recalls the fact that any marked bodily disturbance in infants is apt to show abnormalities in urinary findings. Thus the greater majority of mild and severe gastro-intestinal diseases along with most pulmonary diseases show small amounts of albumin in the urine, which, however, does not predicate the presence of actual renal disease. Therefore edema in infants cannot be considered as due to nephritis, because small amounts of albumin are found in the urine. Dwight observed and studied a series of 21 cases varying in age from sixteen days to three years. Among the diseased conditions present were malnutrition, 12; bronchopneumonia, 2; pericardial effusion, 1; otitis media, 2; cerebrospinal meningitis, 1;

and 2 were in apparent good health. The edema was general in 4 cases, and in the others was limited to the hands or arms, legs or feet, face or abdomen. The blood examinations showed no pernicious or profound anemia. Albumin was present as a faint trace in 9 out of 19 cases, and a heavy trace in 1 case. It was absent in 9 cases, and sugar was absent in all cases. Seven specimens showed occasional granular or hyaline casts. The duration of the edema varied from three to twenty-one days. There were 7 deaths: From malnutrition, 3; bronchopneumonia, 2; meningitis, 1; and pericarditis, 1. Dwight makes a rough classification of the kind of cases that are apt to show edema. First, difficult digestion and mal-assimilation through toxins inducing vasomotor paralysis, or conditions analogous to the urticarias. Second, in exhaustive conditions, prematurity, marasmus, etc. Third, constitutional diseases as syphilis, tuberculosis, erysipelas, etc. Fourth, angioneuroses of vasomotor origin, 2 of which class occurred in the above series.

Position of the Stomach in Children.—JAMES WARREN SEVER (*Archiv f. Pediatrics*, 1914, xxxi, 38) reports his observations on the position of the stomach in children. These observations were made on a large number of children by means of the bismuth meal and the x-rays. A great diversity of opinion has existed among medical men as to the lower border of the stomach in health. From a great number of opinions the average would be at or just above the level of the umbilicus. It is a commonly stated fact that about one person in five is born with a congenitally defective support of the colon and stomach. Sever shows that in children, at least in 90 cases, the position of the stomach is normally much lower than has been suspected. Sever's method included plates taken after a bismuth meal with the child in the usual erect posture, using the crests of the ilia as a landmark instead of the umbilicus. The averages by age, height, and weight, of the cases were well up to or above Holt's averages for children of similar ages. General conditions and body weight were found to have very little to do with the position of the stomach. No relation could be established in regard to the shape or capacity of the thorax with the degree of ptosis present. A study of the x-ray plates of 83 children, taking the crests of the ilia as landmarks, showed the lower border of the stomach opposite the fourth lumbar vertebra in 25 cases; 9 showed it at the level of the crests, and in 49 cases the lower border was well below the crests, often in the pelvis, as much as 3 or 4 inches below the level of the crests. From this uniformly low position of the stomach in so many cases Sever concludes that the position is about normal for children. Few stomachs presented the so-called normal cow's-horn shape, the most persistent type being that of the sink-drain variety. But one of these children had symptoms referable to its digestive tract and this was due to a dilated colon. To find a stomach low in a child does not necessarily mean that there is a pathological ptosis.

OBSTETRICS

UNDER THE CHARGE OF

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Puerperal Pyemia.—WARNEKROS (*Archiv f. Gynäkologie*, 1912, Band xcvii, Heft 1), reports three interesting cases of puerperal pyemia in which operation proved unavailing, and in which interesting observations upon the nature of the disease were made. He believes that by studying the temperature curve of the patient without other data, that the occurrence of blood infection can be recognized and a fairly good idea obtained as to the severity of the infection and its anatomical spread. When a patient has had fever for some time and a chill occurs, repeated on the following day, and between the chills a very marked remission of temperature, either to or below the normal, one can diagnose local endometritis as the primary cause of the fever, and thrombophlebitis as the cause of the chills, with the entrance of masses of bacteria into the blood. When a patient has had atypical fever for some time, and the fever becomes high and continuous without chills, a direct invasion of bacteria into the uterine veins, either at the placental site or through wounds in the uterine mucosa, may be diagnosed. Bacteriological examination is useful in controlling and correcting clinical data. So long as the endometritis is localized, the blood will be found sterile, and if chills occur, with continuous high fever, bacteria will be found in the blood. In pyemia with thrombophlebitis, bacteria are present in the blood at the beginning or during the chill itself; while in severe puerperal septicemia they are found continuously in the blood. From these observations one may gain indications for treatment. In thrombophlebitis, the blood during the interval between the chills is at least comparatively free from bacteria. This, then, is the favorable time for operation, as the infection is then localized. When bacteria are constantly present in the blood, ligation of the thrombosed pelvic veins may still be of some use in limiting the bacteria which enter the circulation. In one of his cases after ligation of the veins the bacteria disappeared from the blood. In operating upon thrombosed pelvic veins, he believes that the common iliac should be selected. If the thrombosis has extended still higher, the vena cava may be tied. The circulation will practically be restored after even so extensive a ligation. So far as the utility of such an operation is concerned, it can only be of value in cases where the bacteria seem to be thrown into the circulation in great numbers during the chills, and where ligation is followed by the disappearance of germs from the blood.

VEIT (*Zentralblatt f. Gynäkologie*, 1912, No. 11), believes that pyemia may be diagnosed with certainty when a puerperal patient has repeated chills. Abdominal section does not militate against the patient. The danger lies in the fact that the tissues about the thrombosed

veins are already infected, and after ligation are not adequately drained. If possible, operation should be done extraperitoneally so far as possible, the endeavor being to lay open the infected focus freely, as well as to ligate the vein. Where the tissues about the veins are found extensively infiltrated, the operation should be abandoned and hirudin given instead. As regards the time of operation, the earlier it is done the more veins must be tied. When operation is performed late, only those veins should be ligated which are evidently thrombosed. Unless one can outline the vessels clearly operation should not be undertaken. In cases where pyemia is complicated by general infection operation will do no good, but on the other hand will do no harm. In discussion, Fromme has observed both the common iliac veins completely plugged without much interruption in the circulation of the lower extremities. He believes that the common iliac can be tied without danger to the patient. He cited Hartmann's paper, in which he described Trendelenburg's ligation of the inferior vena cava in a puerperal patient suffering from pyemia with staphylococci in the blood, the operation proving successful.

BENTHIN from Winter's clinic in Königsburg, (*Zentralblatt f. Gynäkologie*, 1912, No. 39), comments upon Warnekros's paper, and reports two interesting cases of puerperal pyemia from bacteriological examinations. Both cases on admission seemed hopeless, for after endometritis, pyemia declared itself by chills, and in the vaginal secretion and blood streptococci with weak hemolytic power were found. On the thirteenth day of illness the first chill appeared, and on the twenty-third day an extensive thrombosis of the lower extremity. Two days later a second chill occurred, followed by five others at increasing intervals. Bacteria were present in the blood until the twenty-seventh day of the disease, but in progressively lessened numbers. After three months illness both patients recovered. These cases were treated on purely conservative lines without operative interference, even the examinations being limited as much as possible. The patients were given stimulants and abundant food, as the essential elements in treatment.

FINDLEY (*American Journal of Obstetrics*, December, 1912), reports 7 cases of puerperal thrombophlebitis without operation and with conditions which he believes made operation unjustifiable. In the fatal cases autopsy showed that ligation of the veins would not have prevented the spread of septic infection.

Hebostiotomy.—VAN DE VELDE (*Archiv mens. l'Obstétrique*, January, 1912), would limit hebostiotomy to cases of moderate disproportion between mother and child in which but slight increase in pelvic size would be necessary to bring about delivery, both mother and child being in good condition. He alludes to his previous papers upon the subject for the description of his operations. He believes that the operation has a very limited field. The relative importance of forceps, version, pubiotomy and hebostiotomy, in comparison with Cesarean section, may be inferred from the fact that during the past year no extensive and important paper has appeared upon the former operations. Upon Cesarean section alone, in its different varieties, more than thirty papers of differing value have been published. As regards

technique, interest centres in the comparison between the intra- and extraperitoneal methods. The classic section still holds its place as the most widely useful, thorough and comprehensive, of all forms of delivery. When performed upon patients in good condition, its maternal mortality is between 2 and 3 per cent.; its fetal mortality nil. It enables the operator to recognize abnormal conditions in the pelvis and abdomen which demand attention, and places him in a position to deal successfully with them. It is followed by a speedy convalescence, usually uncomplicated, without the interruption of lactation, and leaves the patient in sound condition for further child-bearing. While it is essentially a hospital procedure in emergencies it may be safely done in private houses. It is an operation for experts, and in their hands is remarkably successful. Its application is steadily extending and evidence is accumulating in favor of its selection in accidental separation of the placenta and in central placenta prævia. While vaginal Cesarean section has its advocates, the majority of operators prefer the abdominal route. The advantages claimed for extraperitoneal section are the avoidance of danger following the opening of the peritoneum, the lessened mortality in septic cases, and the prompt recovery without complications, leaving the patient in good condition for subsequent pregnancy. Its disadvantages are the fact that the peritoneum is often opened, that difficulty is sometimes experienced in delivering the child, that hemorrhage is sometimes considerable, and that the uterus is left adherent to the anterior abdominal wall. Extraperitoneal section is frequently practiced in Germany, but less often in other countries.

GYNECOLOGY

UNDER THE CHARGE OF

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Importance of the Lymphatics in Ascending Renal Infection.—Some extremely interesting experimental work in the determination of the method by which ascending infection of the kidney from involvement of the lower urinary tract occurs have been recently reported by SWEET and STEWART (*Surg., Gyn., and Obst.*, 1914, xvii, 460). In a general way, the conclusions at which they have arrived concur with those reached, by somewhat different routes, by Bauereisen and Sugimura, both of whose work has been previously discussed in this department. Bauereisen demonstrated the existence of a communicating chain of lymphatics, running in and about the ureteral wall, between the bladder and the kidney. Sugimura showed, in a series of autopsy specimens from cases with severe infections of the bladder, that the inflammatory process could be followed up the ureter to the kidney, not, however, by way of the mucosa, which was to all intents and purposes intact, but by way of the *lymphatic channels* in the deeper

portions of the ureteral walls. Sweet and Stewart have attacked the problem by the experimental method. By cutting one ureter, and inserting a length of rubber tubing between the severed ends, they have been able to maintain the patency of the lumen, and at the same time completely sever the lymphatic communication between the bladder and the corresponding kidney. When such an operation was performed, the urethra ligated and cut, and a virulent bouillon culture of colon bacilli injected into the bladder, an infection of the kidney on the non-operated side, with intact ureter, occurred, whereas the kidney into whose ureter the rubber tubing had been inserted remained free. Likewise, when a ureter was severed from the bladder, and passed into the intestinal tract through one of the pancreatic ducts, thus leaving the lumen patent, but the lymphatics not in contact with virulent infection, no ascending infection occurred, but in all cases in which the ureter was implanted directly into the intestine, prompt renal involvement followed. On the other hand, in several instances, the ureter was isolated for a short portion of its course, but its continuity to the bladder not severed. The isolated portion was then dropped as a loop into the intestinal lumen through an incision in the gut wall, this being immediately closed, with great care, not to constrict the ureter either at its point of entrance or emergence from the bowel. Thus, the ureteral lumen was in no way exposed to intestinal organisms, but the lymphatics were, and in every instance infection of the kidney occurred. Finally, in several experiments, sufficient of one pole of the kidney was cut away to freely expose the pelvis, and this was planted directly into the intestinal wall. In most of these cases no general infection of the kidney substance occurred. From these experiments, Sweet and Stewart conclude that it is by means of the lymphatics, and not by means of the ureteral lumen or the bloodvessels, that ascending infection of the kidney occurs; they do not, however, deny the possibility of hematogenous infection secondary to some focus *outside* the genito-urinary tract.

Unusual Uterine Tumors.—Three cases of very rare, embryonic malignant tumors of the uterus are reported in the *Jour. Obst. and Gyn. Brit. Emp.* for January, 1914. Two of these, described by Glynn and Bell, were "rhabdomyosarcomata," occurring in two women, aged respectively sixty-two and seventy-five years. In each instance the patient had had a bloody vaginal discharge for some time, and had then passed a tumor mass *per vaginam*, following which hysterectomy was performed. In the first case the uterus was enlarged to the size of a three-months' pregnancy, due to the presence of a tumor growing from the posterior wall, which showed microscopically a mixture of small spindle and very large oval or round cells, with somewhat peripherally situated nuclei. These latter were found to be in reality embryonic muscle cells, cut transversely; in places a few of these cut longitudinally were seen, showing here distinct transverse striations. This patient died six months after operation, with symptoms suggesting pulmonary metastases, but no autopsy was performed. In the second case the diagnosis was made from histological examination of the spontaneously discharged polypoid mass, and a panhysterectomy was then done. Three months later the patient returned with symptoms

of intestinal obstruction; at re-operation the abdomen was found filled with recurrent masses, and the patient died ten days later. The polypoid mass in this instance showed a mixed-celled sarcoma, with numerous giant cells and embryonic striped fibers. The growth in the extirpated uterus, on the other hand, was composed entirely of mixed-celled sarcomas. In neither of these cases were areas of cartilage, glands, or other types of tissue present. The third case, reported by Murray and Littler, occurred in a woman, aged forty-six years. She, likewise, had noticed for some time an unpleasant watery discharge; upon examination a soft polyp was seen projecting from the cervix, and was removed, shortly after which a panhysterectomy was performed. The patient made a good recovery, and up to the time of the report (three months later) did not show signs of recurrence. Histological examination of both the polyp and the polypoid endometrium in the extirpated uterus showed an extremely complex aggregation of tissues—the stroma showed all gradations from a fibrosarcoma to spindle-celled and round-celled sarcoma; there were no giant-cells, but scattered throughout the tissue were numerous areas of hyaline cartilage and many gland-like spaces, lined by a single layer of columnar epithelium, and much resembling the normal endometrial glands. No striated muscle fibers were found. The neoplastic process appeared to be entirely confined to the endometrium, no invasion of the musculature being demonstrable. The last-described tumor is called by Glynn and Bell an "adenochondrosarcoma;" it undoubtedly belongs, however, to the same general group as the first two, *i. e.*, to the category of mesodermal mixed tumors, which probably arise from displacements of embryonic mesodermal tissue from the lumbar region during early life. The high grade of malignancy of the majority of such neoplasms is well illustrated by the course of the first two cases.

Abdominal Exercise in the Treatment of Dysmenorrhea.—MOSHER (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1297), has been making for a number of years careful clinical and experimental studies of so-called functional dysmenorrhea, and has come to the conclusion that it is in the large majority of cases *congestive* in origin, the chief factors responsible for its production being: (1) the upright position, (2) alteration of the normal type of respiration by disuse of the diaphragm, (3) lack of general muscular development, (4) inactivity during the menstrual period, (5) psychic influences. The long column of blood in the valveless vena cava, associated with lowered general blood-pressure at the time of menstruation, the local blood-pressure in the uterus being raised, however, all tend to produce congestion, which is frequently so excessive as to cause dysmenorrhea. The upright position, lax abdominal muscles, costal instead of diaphragmatic breathing, and constriction of the body by clothing which interferes with the use of the abdominal muscles and diaphragm, all combine to develop and promote this pelvic congestion. To correct this condition, Mosher says she has found the following very simple procedure extremely efficacious: All tight clothing is removed, and the patient is placed on her back, on a level surface, in the horizontal position. The knees are flexed, and the arms are placed at the sides to secure relaxation of the abdominal muscles. One hand is allowed to rest on the abdominal wall

without exerting any pressure, to serve as an indicator of the amount of movement. The woman is then directed to see how high she can raise the hand by lifting the abdominal wall; then to see how far the hand will be lowered by the voluntary contraction of the abdominal muscles, the importance of this contraction being especially emphasized. This exercise is repeated ten times, night and morning, in a well-ventilated room. The patient is warned to avoid jerky movements, and to strive for a smooth, rhythmical raising and lowering of the abdominal wall. Mosher says that in a large number of cases she has seen a disappearance of all pain, and in many instances a reduction in excessive flow will occur after the institution of this simple regimen. She believes that many women would be far better off if they kept up a greater degree of bodily activity throughout the period than is their custom, although of course, this should not be overdone, and in schools and colleges it would certainly be unwise in most instances to permit the girls to continue all their regular gymnastics and athletics at this time. A most important point, in Mosher's opinion, is to bring about an alteration of the morbid attitude of women themselves toward the menstrual function; as she very truly remarks, "If every young girl was taught that menstruation is not normally a 'bad time,' and that pain or incapacity at that period is as discreditable and unnecessary as bad breath due to decaying teeth, we might almost look for a revolution in the physical life of woman."

Relationship of Gynecology to Psychiatry.—As is well known, Bossi and a few followers are strong believers in the theory that many psychopathic conditions, occurring in women, have their origin in faulty functioning of the genital organs, such as alterations in the internal secretory activities of these organs, the condition of retroverted uterus, with metritis, being, in Bossi's opinion, especially important in this respect. As has been previously discussed in these pages, Bossi claims that many cases of suicidal mania and other forms of insanity can be permanently cured by the performance of suitable gynecological manipulations or operations. A most energetic refutation of Bossi's entire idea has been recently put forth by Siemerling (*Monatsschr. f. Geb. u. Gyn.*, 1914, xxxix, 269), who claims that not only are the former's theories with regard to the origin of psychopathic conditions utterly without foundation in fact, but that examination of records of a large series of cases shows that recovery occurred in as large a proportion of women suffering from psychic disorders upon whom no gynecological treatment was carried out as of those who were treated according to Bossi's principles. He emphasizes, moreover, the fact that many psychoses, such as melancholia, amentia, manic-depressive types, etc., tend to spontaneous recovery, and this, following, in some instances gynecological treatment or operation, may easily give the impression of having been the result of such treatment. Siemerling takes the ground that in the routine examination of every psychopathic patient the genital organs should be taken into consideration, as all other organs of the body, and any conditions found which in a mentally normal individual would require treatment, should be treated just as they would be in such an individual without regard to the mental condition; beyond this, however, he does not think that gynecology has any legitimate field in the treatment of cases of mental disease.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF
J. SOLIS-COHEN, M.D.,
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Tumor of the Soft Palate Consisting Mainly of Salivary Gland Tissue.
—GUTHRIE (*Jour. Laryn., Rhinol., and Otol.*, February, 1914), reports and depicts this case, which consisted of a pear-shaped tumor hanging from the right side of the soft palate of a lad, aged eight years. When cut through the middle after removal the tumor measured 9 mm. longitudinally and 6 mm. transversely, and was found to consist of a mixed salivary gland of the submaxillary type. The reporter had not been able to discover any record of a similar case.

Tonsillectomy in the Upright Position Under Ether.—ROBERTS describes and depicts (*Laryngoscope*, February, 1914) his method of performing tonsillectomy in the upright position under ether, using a Whitehead gag and administering the ether through one of the nasal passages.

Foreign Body (Halfpenny) in an Esophagus of a Child for Eight Years.
—PORTER (*Jour. Laryn., Rhinol., and Otol.*, February, 1914), reports the case of a child who had swallowed a halfpenny at the age of four years and retained it in his esophagus for eight years. An x-ray photograph showed its presence in the esophagus between the fifth and sixth dorsal vertebræ. An attempt to seize it with forceps under esophagoscopic inspection failed, and the coin slipped out of sight into the stomach. No ulceration or lesion of any kind could be detected in the walls of the esophagus at the point of detention.

Suspension Laryngoscopy in Children.—ALBRECHT (*Jour. Laryn., Rhinol., and Otol.*, February, 1914) states that suspension laryngoscopy in children is much simpler than in adults. The reasons for this he ascribes partly to the upright position of the epiglottis, which often permits of a satisfactory view as soon as the base of the tongue is pressed upon, and partly to the slender build of the neck characteristic of childhood. He states that clinically the procedure has rendered more certain: (1) the removal of the larger infantile nodes ("screamer's nodes"), analogous to the singer's nodes of adult life, and ascribed to habitual crying or screaming; (2) the operative treatment of laryngeal tuberculosis; (3) the operative treatment of papilloma, which he considers its great field, and of which he mentions nine cases thus treated. To these three procedures he adds a fourth, enucleation of the tonsils, stating that in operating under narcosis, and with the head dependent; suspension gives a first-rate view of the tonsillar region, so that enucleation can be effected in a few minutes under the strictest visual control.

Extirpation of the Arytenoid Cartilage in Laryngeal Stenosis.—IWANOFF discusses (*Revue Hebdomadaire de Laryngologie, d'Otologie, et de Rhinologie*, February 21, 1914), dyspnea produced in stenosis of the larynx due to immobilized median position of the vocal cords. He recommends extirpation of the arytenoid cartilage in order to secure and maintain a larger glottis and thus dispense with the permanent use of the tracheal cannula. The operation is described in detail and one case is narrated in which, after considerable tribulation, a satisfactory result ensued.

Resection of the Vocal Cords in Laryngeal Stenosis.—IWANOFF reports (*Revue Hebdomadaire de Laryngologie, d'Otologie, et de Rhinologie*, February 28, 1914) 4 cases of laryngeal stenosis from vocal cords in median position in which he has practised with success, resection of the vocal cords so as to allow the patient to breathe without the use of the cannula. (This is an operation long practised by veterinarians to overcome "roaring" in abductor paralysis of the vocal cords in horses). Iwanoff states that the voice is not much impaired, and sometimes it is even better than is found in many cases of chronic laryngitis.

Histological Examination of the Superior Laryngeal Nerve After Injections of Alcohol.—LANNOIS AND BÉRIEL report (*Revue Hebdomadaire de Laryngologie, d'Otologie, et de Rhinologie*, March 7, 1914) 9 cases in which they examined the superior laryngeal nerve in patients who succumbed a few days after injections of alcohol for the relief of pain in laryngeal tuberculosis. These examinations were controlled by similar examinations in cases of laryngeal tuberculosis who had not been subjected to injections. While the results are not very positive, it may be said that the alcoholic injections but little modified the nerve trunk, because in a number of cases histological differences were rarely to be detected between nerves injected and nerves not injected. It was suggested that this circumstance might indicate that the alcohol was rarely introduced into the nerve itself. On the other hand, it might be inferred that this injection into the nerve does not appear to be indispensable for the therapeutic result. It might be mentioned that when histological modification had been noted it was always periaxial.

HYGIENE AND PUBLIC HEALTH

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Uta.—STRONG, TYZZER, BRUES, SELLARDS, AND GASTIABURU (*Journal of the American Medical Association*, November 8, 1913, lxi, 1713) report upon *uta*, a disease which has existed in Peru since prehistoric times, and the

lesions of which have been supposedly depicted on the ancient "huacos" of the Incas. It has been stated by various authorities that the disease represented a form of syphilis, or one of prehistoric leprosy, or a special form of lupus vulgaris. In recent years two extensive monographs on the subject have appeared from Peru, one by Tamayo in 1908 and the other by Palma in 1909. Tamayo regarded the disease as a special form of lupus vulgaris. Palma concluded that it was a specific disease which was not to be confounded with other South American maladies, and that it was not a form of tuberculosis. The present investigation showed that uta is due to a species of *Leishmania*. The flagellate stage of the organism was obtained, and animals were successfully inoculated from a human case. In both Surco and Otao (the latter town deriving its name from the prevalence of the disease there) a large proportion of the inhabitants are either afflicted with the disease or show the disfiguring scars which have resulted from a previous attack, on the face, arms, or legs.

Verruga Peruviana and Oroya Fever.—STRONG, TYZZER, BRUES, SELLARDS, and GASTIABURN, (*Journ. Amer. Med. Assoc.*, November 8, 1913, lxi, 1713) report upon two distinct diseases, verruga peruviana and oroya fever, which were formerly considered to be merely different stages of one disease. The disease was supposed to begin with the oroya fever stage, also known as the *fièvre grave* of Carrion, and if the individual did not die in this stage then the eruptive or verruga stage was said to follow. If the eruption was generalized and abundant, it was stated the individual would surely recover. In the chronic or mild type of the disease the severe initial fever was supposed to occur. It appears that the reason for considering the two diseases as merely different stages of one disease was based particularly upon the fact that in 1885 Daniel Carrion, a Peruvian medical student, in trying to solve problems in relation to the etiology of the affection, inoculated himself on both arms with material from a verruga nodule. It is related that twenty-three days later he began to suffer with symptoms of oroya fever, from which complaint he died sixteen days later. However, no accurate record of Carrion's symptoms is available, and no accurate record of the autopsy performed. It has since been suggested that he died of typhoid fever. Numerous organisms have been described in connection with the etiology of verruga peruviana and its so-called oroya fever stage. Barton has described a bacillus as the cause of the fever stage, which was later shown to be a paratyphoid bacillus. Later he reported the presence of bodies in the red-blood corpuscles, which he thought were protozoa. By latter observers these were generally regarded as products of cell degeneration. A number of other investigators have found paratyphoid bacilli in the blood in the fever stage, while others found acid-fast bacilli in the lesions from the skin. A species of *Leishmania* and one of chlamydozoa have also been regarded as the etiological factor in verruga. Thus at the time the present investigations were undertaken, the etiology of verruga peruviana and its so-called oroya fever stage was not determined. It was first shown that verruga peruviana and oroya fever represent two distinct diseases; that verruga was due to a virus which was transmitted to the rabbit's testicle, and particularly to monkeys, by cutaneous inoculation, while

oroya fever was due to a parasite of the red-blood corpuscles. The parasite in oroya fever produces in man an irregular fever, and in severe infections a rapid and very pernicious form of anemia which results in extreme prostration and frequently in death. The parasites were observed in both fresh and stained-blood preparations. They were either rounded or rod-shaped, the rods measuring from one to two microns in length, and the rounded forms from three-tenths to one micron in diameter. They occurred singly and in pairs, end to end, and also in chains. In preparations stained in Giemsa, rods often showed a deeply red staining granule at the ends, while the rest of the rod frequently assumed a more bluish tint. The organism resembles in some of its characteristics those described for anaplasma or certain species of theileria, as well as for those given for two species of grahamella by Brumpt, but in other respects it differed considerably from these, and was therefore classified in a new genus Bartonella, the name of Bartonella bailliformis being given to the organism of oroya fever.

Autopsy Findings in the Case of Typhoid Bacillus Carrier.—MERSCHMIDT (*Zeit. f. Hygiene*, 1913, lxxv, 411) reports the circumstances of an aged, mentally deficient woman, who in August, 1907, suffered from typhoid fever, following which she became a chronic carrier. In the first year subsequent to her typhoid attack, not only the feces but also the urine was infected. The urine then cleared up and the feces continued to show intermittently positive results until the time of her death in 1912. Shortly after the original attack the patient had a purulent pleurisy, from which typhoid bacilli were cultivated. The bacilli persisted, however, in the pleuritic exudate for a few days only. At the autopsy, typhoid bacilli were found not only in the bile but also the wall of the gall-bladder, in the liver, in the neighborhood of the great bloodvessels, in the papillae of one kidney, and also in one suprarenal capsule. As far as the latter organ is concerned, however, the condition is to be looked at as a secondary typhoid invasion of an old tubercular focus. As was to be expected, furthermore, the bacilli were cultivated also from various portions of the intestinal tract. During life, treatment had been attempted with yoghurt, atoxylsaurem quecksilber, and with typhoid-immune serum (Kraus), but without result.

ERRATA.—The observations of Uhlenhuth and Mulzer (*Arb. a. d. Kais. Gesundh. Aml.*, 1913, xlv, 307), abstracted on page 447 of the March issue of the JOURNAL, were made upon rabbits, not upon dogs. The same correction applies to the observations of Prausnitz and Stem (*Zentralbl. f. Bakteriologie*, 1913 lxi, 545), abstracted on page 448 of the same issue.

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